

TCACGTAAAA AGGTATCTA GAATTATGAT GATTACTCTG CGCAAACTTC CTCTGGCGGT TGCCGTGCGA GCGGGCGTAA TGTCTGCTCA GGCCATGGCC
AGTGCATTTT TCCCATAGAT CTTAATACTA CTAATGAGAC GCGTTTGAAG GAGACCGCCA ACGGCAGCGT CGCCCGCATT ACAGACGAGT CCGGTACCGG
MetMe tileThrLeu ArgLysLeuP roLeuAlaVa lAlaValAla AlaGlyValM etSerAlaGl nAlaMetAla
^Start of lamB signal sequence

GGTCCCGAAA CTCTGTGGG TGCTGAACTG GTTGACGCTC TGCAGTTCGT ATGTGGTGAT CGAGGCTTCC TGTTCACAA ACCGACTGGG GCTGGATCCT
CCAGGGCTTT GAGACACGCC ACGACTTGAC CAAGTTCGAG ACGTCAAGCA TACACCACTA GCTCCGAAGG ACAAGTTGTT TGGCTGACCC CGACCTAGGA
GlyProGluT hrLeuCysGl yAlaGluLeu ValAspAlaL euGlnPheVa lCysGlyAsp ArgGlyPheL euPheAsnLy sProThrGly AlaGlySerSer
^Start of IGF-I (Y24L, Y31A)

CCTCTCGTCG TGCTCCCCAG ACTGGTATTG TTGACGAATG CTGCTTTCGT TCTTGGGACC TGCGTCGTCT GGAAATGTAT TGGCTCCCC TGAACCCCGC
GGAGAGCAGC ACGAGGGGTC TGACCATAAC AACTGCTTAC GACGAAAGCA AGAAGCTGG ACGCAGCAGA CCTTTACATA ACGCGAGGGG ACTTTGGGCG
SerArgAr gAlaProGln ThrGlyIleV alAspGluCy sCysPheArg SerCysAspL euArgArgLe uGluMetTyr CysAlaProL eulysProAla

TAAATCTGCT TAGAAGCTCC TAACGCTCGG TTGCCCGCCGG GCGTTTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT AATGCGGTAG
ATTTAGACGA ATCTTCGAGG ATTGCGAGCC AACGGCGGCC CGCAAAAAAT AACAAATTGAG TACAAACTGT CGAAATAGTAG CTATTGAAA TTACGCCCATC
LysSerAla Am*

Nucleotide and Amino Acid Sequence of the lamB Signal Sequence and IGF-I (Y24L, Y31A)

FIG. 1

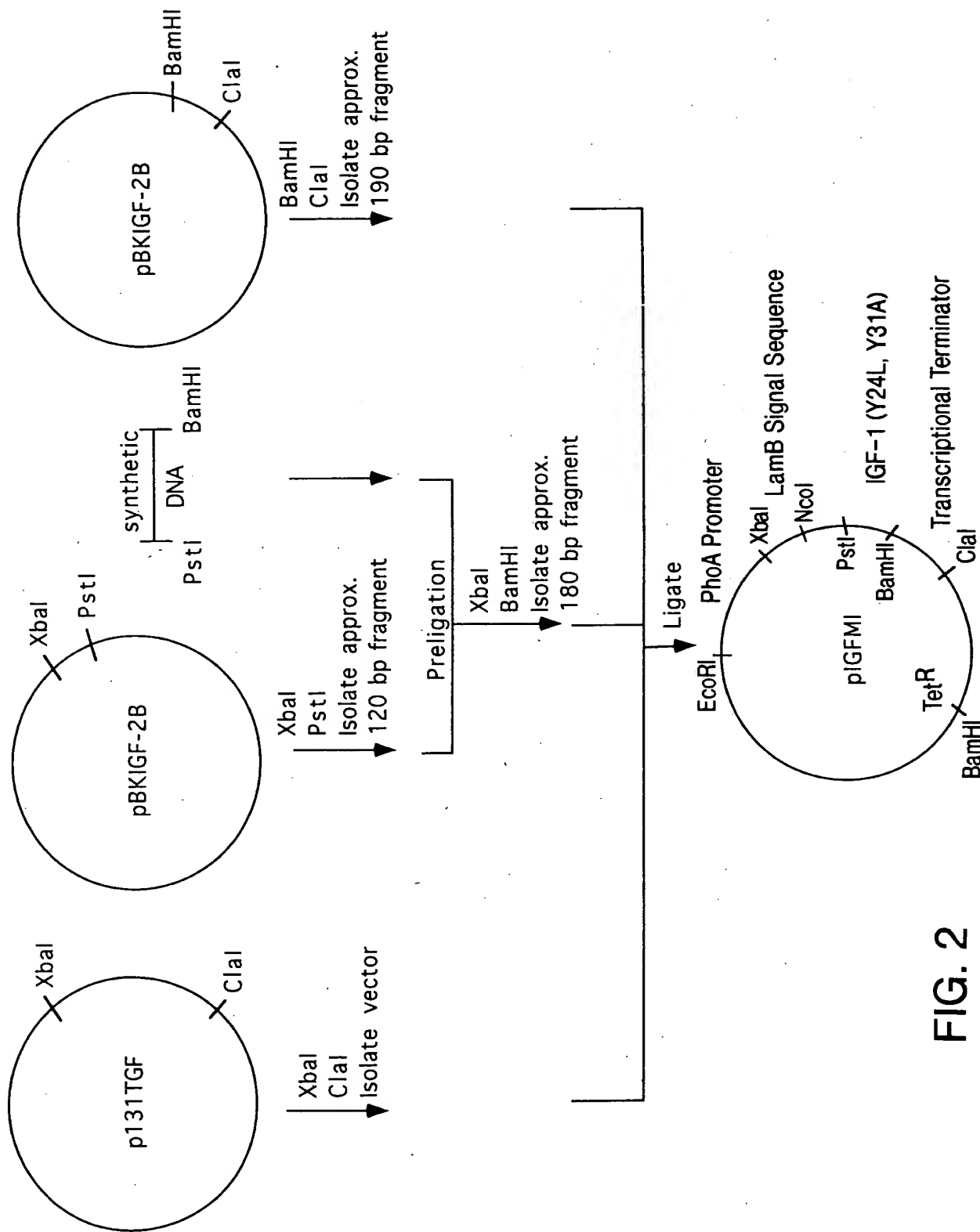


FIG. 2



plasmid IGfMI

length: 5115 (circular)

```
1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCTG TACTTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTTCT TCACAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACACGG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGGTTACGA AGCGTTATAC CCGGTTTTAC TGGTTGTCGC CAACTAACTA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCACTA
CCCCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCAACA GCTGTCAATA AGTTGTCACG GCCGAGACTT ATAGTCGCTT TGTGTTTATT TTTTAATGTA TTTGTAACCTA GTACGCAAGT
TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CCGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AACATTGAT CATGCCGTCA

401 TCACGTAAAA AGGTATCTA GAATTATGAT GATTACTCTG CGCAAACTTC CTCTGGCGGT TGCCCTCGCA GCGGGCGTAA TGTCTGCTCA GGCCATGGCC
AGTGCAATTT TCCCATAGAT CTTAATACTA CTAATGAGAC GCGTTTGAAG GAGACCGCCA ACGGCAGCGT CGCCCGCAAT ACAGACGAGT CCGGTACCGG

1 MetMe tilethrLeu ArgLysLeup roLeuAlaVal AlaGlyValM etSerAlaGl nAlaMetAla

501 GGTCGCGAAA CTCTGTGCGG TGCTGAACCTG GTTGACGCTC TGCAAGTTCGT ATGTGGTGAT CGAGGCTTCC TGTTCAACAA ACCGACTGGG GCTGGATCCT
CCAGGGCTTT GAGACACGCC ACGACTTGAC CAATCGGAG ACGTCAAGCA TACACCACCTA GCTCCGAAGG ACAAGTTGTT TGGCTGACCC CGACCTAGGA

26 GlyProGluT hrLeuCysG1 yAlaGluLeu ValAspAlaL euGlnPheVa lCysGlyAsp ArgGlyPheL eupHeAsnLy sProThrGly AlaGlySerSer

601 CCTCTCTGCG TGCTCCCCAG ACTGGTATTG TTGACGAATG CTGCTTTCGT TCTTGCAGCC TGCGTCGTCT GGAATGTAT TGCGCTCCCC TGAACCCCGC
GGAGAGCAGC ACGAGGGGTC TGACCATAAC AACTGCTTAC GACGAAAGCA AGAACGCTGG ACGCAGCAGA CTTTACATA ACGCGAGGGG ACTTTGGGCG

60 SerArgAr gAlaProGln ThrGlyIleV alAspGluCy sCysPheArg SerCysAspL euArgArgLe uGluMetTyr CysAlaProL euLysProAla

701 TAAATCTGCT TAGAAGCTCC TAACGCTCGG TTGCCGCGCG GCGTTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT AATGCGGTAG
ATTTAGACGA ATCTTCGAGG ATTGCGAGCC AACGGCGGCC CGCAAAAAT AACAAATTGAG TACAAACTGT CGAATAGTAG CTATTGAAA TTACGCCATC

93 LysSerAla Am*

801 TTTATCAcAG TTAAATTGCT AACCGAGTCA GGCACCGTGT ATGAAATCTA ACAATGCGGT CATCGTCATC CTCGGCACCG TCACCCCTGA TGCTGTAGGC
AAATAGTGTC AATTTAACGA TTGCGTCAGT CCGTGGCACA TACTTTAGAT TGTTACCGGA GTAGCAGTAG GAGCCGTGGC AGTGGACCT ACGACATCCG

901 ATAGGCTTGG TTATGCCGGT ACTGCCGGG CTCTTGCGGG ATATCGTCCA TTCCGACAGC ATCGCCAGTC ACTATGGCGT GCTGCTAGCG CTATATGCGT
TATCCGAACC AATACGGCCA TGACGGCCCG GAGAACGCC TATAGCAGGT AAGGCTGTCTG TAGCGGTCTAG TGATACCGCA CGACGATCGC GATATACGCA

1001 TGATGCAATT TCTATGCGCA CCGGTTCTCG GAGCACTGTC CGACCGCTTT GGCGCGCGCC CAGTCCTGCT CCGTTCCGCTA CTTGGAGCCA CTATCGACTA
ACTACGTTAA AGATACGCGT GGGCAAGAGC CTCGTGACAG GCTGGCGAAA CCGCGCGCGG GTCAGGACGA GCGAAGCGAT GAACCTCGGT GATAGCTGAT
```

FIG. 3A



1101 CGCGATCATG GCGACCACAC CCGTCCTGTG GATCCTCTAC GCCGGACGCA TCGTGCCCGG CATCACCCGG GCCACAGGTG CGGTTGCTGG CGCCTATATC
GCGTAGTAC CGCTGGTGTG GGCAGGACAC CTAGGAGATG CCGCCTGCGT AGCACCGGCC GTAGTGCCG CGGTGTCCAC GCCAACGACC GCGGATATAG

1201 GCCGACATCA CCGATGGGGA AGATCGGGCT CGCCACTTCG GGTTCATGAG CGCTTGTTTC GCGTGGGTA TGGTGGCAGG CCCCCTGGCC GGGGGACTGT
CGCGTGTA GTGCTACCCCT TCTAGCCCCGA GCGGTGAAGC CCGAGTACTC CCGACAAAG CCGCACCCAT ACCACCGTCC GGGGCACCGG CCCCCTGACA

1301 TGGGGCCCAT CTCCTTGCA TGCACATTCC TTGCGCGCGG GGTGCTCAAC GGCCTCAACC TACTACTGG CTGCTTCTTA ATGCAGGAGT CGCATAAGGG
ACCCCGGGTA GAGGAACGTA CGTGTAAGG AACGCGCGG CACAGAGTGG CCGAGTTGG ATGATGACCC GACGAAGGAT TACGTCTCA GCGTATTCCC

1401 AGAGCGTCGA CCGATGCCCT TGAGAGCCTT CAACCCAGTC AGCTCCTTCC GGTGGGCGG GGCATGACT ATCGTCGCCG CACTTATGAC TGTCTTCTTT
TCTCGCAGCT GGCTACGGGA ACTCTCGGAA GTTGGGTGAG TCGAGGAAG CACCCCGCG CCGTACTGA TAGCAGCGG GTGAATACTG ACAGAAGAAA

1501 ATCATGCAAC TCGTAGGACA GGTGCGCGCA GCGCTCTGG TCAATTTTCG CGAGGACCGG TTTCGCTGGA GCGCGACGAT GATCGGCCCTG TCGCTTGCGG
TAGTACGTTG AGCATCCTGT CCACGCGCGT CCGGAGACCC AGTAAAGCC GCTCCTGGG AAAGCGACCT CCGCTGCTA CTAGCCGGAC AGCGAACGCC

1601 TATTCGGAAT CTTGCACGCC CTCGCTCAAG CTTTCGTAC CTTTCGTAC TGGTCCCGG ACCAAACGTT TCGGCGAGAA GAGGCCATT ATCGCCGGCA TGGCGGCCGA
ATAAGCCTTA GAACGTGCGG GAGCGAGTTC GGAAGCAGTG ACCAGGCGG TGGTTTGCAA AGCCGCTCTT CGTCCGGTAA TAGCGGCCGT ACCGCCGGCT

1701 CGCGCTGGG TACGTCTTG TGGGTTTGC GACGCGAGG TGGATGGCT TCCCATTTAT GATTTCTTC GCTTCCGGG GCATCGGGAT GCGCGCGTTG
GCGGACCCG ATGAGAACG ACCGCAAGCG CTGCGTCCG ACTTACCGA AGGGTAATA CTAAGAAGAG CGAAGGCCG CGTAGCCCTA CCGCGCAAC

1801 CAGGCCATGC TGTCCAGGCA GGTAGATGAC GACCATCAGG GACAGTTCA AGGATCGTC GCGGCTCTTA CAGCCTAAC TTCGATCACT GGACCGCTGA
GTCCGGTACG ACAGTCCGT CCATCTACTG CTGGTAGTCC CTGTGAAAT TCTTAGCGG AGCCGAGAA GTTCGGATTG AAGCTAGTGA CCTGGCGACT

1901 TCGTCACGG GATTTATGCC GCCTCGSCGA GCACATGGAA CCGGTTGGCA TGGATTGTAG GCGCGGCCCT ATACCTTGTG TGCCTCCCC CGTTGCGTGC
AGCAGTGCCG CTAATACGG CCGAGCCGT CGTGACCTT GCCCAACCGT ACCTAACATC CCGCGCGGA TATGGAACAG ACGGAGGGG GCAACGCGAG

2001 CCGTGCAATG AGCGGGCCA CCTCGACCTG AATGGAAGC GCGGACCTT CGCTAACGGA TTCACCACTC CAAGAATTGG AGCCAATCAA TTCTTGCGGA
GCCACGTACC TCGGCCCGGT GGAGCTGGAC TTACCTTCGG CCGCGGTGGA GCGATTGCTT AAGTGTGAG GTTCTTAACC TCGGTTAGTT AAGAAGCCTT

2101 GAACTGTGAA TCGGCAAAACC AACCTTGGC AGAACAATC CATCGCTCC GCCATCTCCA GCAGCCGAC GCGGCGCATC TCGGGCAGG TTGGGTCTTG
CTTGACACTT ACGCGTTGG TTGGGAACCG TCTTGATAG GTAGCGCAGG CCGTAGAGGT CCGCGCGTG CCGCGCGTAG AGCCGTCG AACCAGGAC

2201 GCCACGGGTG CGCATGATCG TGCTCTGTG GTTGAGGACC CCGCTAGGCT GCGCGGGTTG CTTACTGGT TAGCAGAATG AATCACCGAT ACGCGAGCGA
CGGTGCCCC GCGTACTAGC ACGAGGACAG CAATCTCTGG GCCGATCCGA CCGCCCCAAC GGAATGACCA ATCGTCTTAC TTAGTGGCTA TGGCTCGCT

2301 ACGTGAAGCG ACTGCTGCTG CAAAACGTCT GCGACCTGAG CAACAACATG AATGGTCTT GGTTCCTGTG TTTCTGTAAG TCTGGAACG CGGAAGTCAG
TGCACCTGCG TGACGACGAC GTTTTGACAG CGCTGGACTC GTTGTGTAC TTACCAGAAG CCAAAGGCAC AAAGCATTT AGACCTTTG GCTTCAGTC

2401 CGCCCTGCAC CATTATGTT CCGATCTGCA TCGCAGGATG TCGCTGGCTA CCCTGTGGA CACCTACATC TGTATTAACG AAGCGCTGG ATTGACCCCTG
GCGGACGCTG GTATATACAG GCCTAGACGT AGCGTCTAC GAGCACCTT GGGACACCTT GTGGATGTAG ACATAATTG TCGCGGACCG TAACCTGGAC

FIG. 3B



2501 AGTGATTTT CTCTGGTCC GCGCATCCA TACGCCAGT TGTTTACCT CACAACGTT CAGTAACCG GCATGTTT CATCAGTAAC CCGTATCGTG
TCACTAAAA GAGACCAGG CGGCGTAGG ATGGCGGTCA ACAATGGGA GTGTTGCAAG GTCATTGGCC CGTACAAGTA GTAGTCATTG GGCATAGCAC

2601 AGCATCTCT CTCGTTTTCAT CCGTATCAT ACCCCCATGA ACAGAAATTC CCCCTTACAC GGAGGCATCA AGTGACCAAA CAGGAAAAAA CCGCCCTTAA
TCGTAGGAGA GAGCAAAGTA GCCATAGTAA TGGGGTACT TGTCTTTAAG GGGGAATGT CCTCCGTAGT TCACTGGTTT GTCCCTTTT GGCGGGAATT

2701 CATGGCCGC TTTATCAGAA GCCAGACATT AACGTTCTG GAGAAACTCA ACAGAGTGA CCGGATGAA CAGGCAGACA TCTGTGAATC GCTTCACGAC
GTACCGGCGG AATAGTCTT CCGTCTGTAA TTGCGAAGAC CTCTTTGAGT TGCTCGACCT GCGCTACTT GTCCGTCTGT AGACACTTAG CGAAGTGTG

2801 CACGCTGATG AGCTTTACCG CAGCTGCCTC GCGGTTTCG GTGATGACGG TGAAAACTC TGACACATGC AGCTCCCGA GACGGTCACA GCTTGTCTGT
GTGCGACTAC TCGAAATGCC GTCGACGGAG CGCGAAAGC CACTACTGCC ACTTTTGAG ACTGTGTAG TCGAGGGCCT CTGCCAGTGT CGAACACAGACA

2901 AAGCGGATGC CCGGAGCAGA CAAGCCCGTC AGGCGCGTC AGCGGTGTT GCGGGGTGTC GGGCGGAGC CATGACCCAG TCACGTAGCG ATAGCGGAGT
TTCCGCTAGG GCCCTCGTCT GTTCGGGCAG TCCCGCGCAG TCGCCACAA CCGCCACAG CCGCGGTGTC GACTGGGTGTC AGTGATCGC TATCGCCTCA

3001 GTATACTGC TTAACATATG GGCATCAGAG CAGATTGTAC TGAGAGTGCA CCATATGCGG TGTGAAATAC CGCACAGATG CGTAAGGAGA AAATACCGCA
CATATGACCG AATTGATACG CCGTAGTCTC GTCTAACATG ACTCTACGT GGTATACGCC ACACCTTTATG CCGTGTCTAC GCATTCTCT TTTATGGCGT

3101 TCAGCGCTC TTCGCTTCC TCGCTCACTG ACTCGTGGC CTGCGTGGT CCGCTGCGG GAGCGGTATC AGCTCACTCA AAGCGGTAA TACGGTTATC
AGTCCCGCAG AAGCGAAGG ACGGAGTAC TGAGCGACG GAGCCAGCA GCCGACCGG CTCGCCATAG TCGAGTGTG TCCCGCATT ATGCCAATAG

3201 CACAGAAATCA GGGATAACG CAGGAAAGAA CATGTAGCA AAAGGCCAG AAACCGTAA AAGCGCGCT TGCTGGCGT TTTCCATAGG
GTGCTTAGT CCCCTATTGC GTCCCTTCTT GTACACTCGT TTTCCGGTC CTTGGCATTT TTCCGGCGCA ACGACCGCAA AAAGGTATCC

3301 CTCGCCCCC CTGACGAGCA TCACAAAAAT CGACGCTCAA GTCAGAGTG GCGAAACCCG ACAGGACTAT AAAGATACCA GCGGTTTCCC CCTGGAAGCT
GAGCGGGGG GACTGCTCGT AGTGTTTTTA GCTGCGAGT CAGTCTCCAC CGCTTTGGC GTCTTGATA TTTCTATGT CCGCAAAGG GACCTTCGA

3401 CCCTCGTGG CTCTCCTGTT CCGACCCCTGC CGCTTACCG ATACCTGTCC GCCTTTCTCC CTTGGGGAAG CGTGGCGCTT TCTCATAGCT CACGCTGTAG
GGGAGCACGC GAGAGGACAA GGCTGGGACG GCGAATGGCC TATGGACAGG CGGAAAGAGG GAAGCCCTTC GCACCGCGAA AGAGTATCGA GTGCGACATC

3501 GTATCTCAGT TCGGTGTAGG TCGTTCGCTC CAAGCTGGG TGTGTGACG AACCCCGCT TCAGCCCGAC CGTGGCGCT TATCCGGTAA CTATCGTCTT
CATAGAGTCA AGCCACATCC AGCAAGCGAG GTTCGACCCG ACACACGTG TTGGGGGCA AGTCGGGCTG GCACCGCGGA ATAGGCCATT GATAGCAGAA

3601 GAGTCCAACC CCGTAAGACA CGACTTATCG CCACTGGCAG CAGCCACTGG TAACAGATT AGCAGAGCGA GGTATGTAGG CCGTGTACAG GAGTTCTTGA
CTCAGGTTGG GCCATTCTGT GTGAATAGC GGTGACCGTC GTGCTGTGACC ATTGTCTTAA TCGTCTCGCT CCATACATCC GCCACGATGT CTCAAGAACT

3701 AGTGGTGGC TAACTACGGC TACACTAGAA GGACAGTATT TGGTATCTGC GCTCTGTGA AGCCAGTTAC AGCCGAAA AGAGTTGTA GCTCTTGATC
TCACCACCGG ATTGATGCC ATGTATCTT CCGTGCATAA ACCATAGACG CGAGACGACT TCGGTCAATG GAAGCCTTTT TCTCAACCAT CGAGAACTAG

FIG. 3C



3801 CGGCAACAA ACCACCGCTG GTAGCGGTGG TTTTCTTGTG TGCAAGCAGC AGATTACGG CAGAAAAAA GGATCTCAAG AAGATCCTTT GATCTTTTCT
GCCGTTTGT TGGTGGCGAC CATCGCCACC AAAAAACAA ACGTTCTGTC TCTAATGCGC GTCCTTTTCT CCTAGAGTTC TTCTAGGAAA CTAGAAAAA
3901 ACGGGGCTG ACGCTCAGTG GAACGAAAA TCACGTTAAG GGATTTTGGT CATGAGATTA TCAAAAAGGA TCTTCACCTA GATCCTTTTA AATTAAAAA
TGCCCCAGAC TCGAGTCTAC CTTGCTTTTG AGTGCAATTC CCTAAAACCA GTACTCTAAT AGTTTTCCT AGAAGTGGAT CTAGAAAAA TTAATTTTA
4001 GAAGTTTAA ATCAATCTAA AGTATATATG AGTAACTTG GTCTGACAGT TACCAATGCT TAATCAGTGA GGCACCTATC TCAGCGATCT GTCTATTTCG
CTTCAAAAT TAGTTAGATT TCATATATAC TCATTTGAC CAGACTGTCA ATGGTTACGA ATTAGTCACT CCGTGGATAG AGTCGTAGA CAGATAAAGC
4101 TTCATCCATA GTTGCTGAC TCCCCGTCGT GTAGATAACT ACGATACGG AGGGCTTACC ATCTGGCCC AGTGCTGCAA TGATACCGC AGACCCACGC
AAGTAGGTAT CAACGGACTG AGGGGCAGCA CATCTATTGA TGCTATGCC TCCCGAATGG TAGACCGGG TCACGACGTT ACTATGCGC TCTGGGTGCG
4201 TCACCGGCTC CAGATTTATC ACCAATAAC CAGCCAGCCG GAAGGGCCGA GCGCAGAAGT GGTCTGCAA CTTTATCCGC CTCCATCCAG TCTATTAAAT
AGTGGCCGAG GTCTAAATAG TCGTTATTG TCGGTCGCGC CTTCCCGGT CCGCTCTCA CCAGGACGTT GAAATAGGCG GAGGTAGGTC AGATAATTAA
4301 GTTGCCGGA AGCTAGAGTA AGTAGTTCG CAGTTAATAG TTTGCGCAAC GTTGTGCCA TTGCTGCAGG CATCGTGGTG TCACGCTCGT CGTTTGGTAT
CAACGGCCCT TCGATCTCAT TCATCAAGCG GTCAATTATC AAACGCGTTG CAACAACGTT AACGACGTC GTAGCACCA AGTGCGAGCA GCAAACCAT
4401 GGCTTCATC AGCTCCGGT CCCAACGATC AAGCGAGTT ACATGATCCC CCATGTTGTG CAAAAAGCG GTTAGCTCCT TCGGTCTCC GATCGTTGTC
CCGAAGTAAG TCGAGGCCAA GGGTTGCTAG TTCCGCTCAA TGACTAGGG GGTACACAC GTTTTTTCG CAATCGAGGA AGCCAGGAG CTAGCAACAG
4501 AGAAGTAAGT TGGCCGAGT GTTATCACTC ATGGTTATGG CAGCACTGCA TAATCTCTT ACTGTCAAG CATCCGTAAG ATGCTTTTCT GTGACTGGTG
TCTTCATTCA ACCGGCGTCA CAATAGTGAG TACCAATACC GTCGTGACGT ATTAAGAGAA TGACAGTACG GTAGGCATT TACGAAAAA CACTGACCAC
4601 AGTACTCAAC CAAGTCATT TGAGATAGT GTATGCGCG ACCGAGTTG TCTTGCCCG TCTTCAACG AGAACGGCC GCAGTTGTG CCGGTGTAT CGTCTTGAAA
TCATGAGTTG GTTCAGTAAG ACTCTATCA CATAAGCCG TGCTCAACG AGAACGGCC GCAGTTGTG CCGGTGTAT CCGGTGTAT CGTCTTGAAA
4701 AAAAGTGCT ATCATTTGAA AACGTTCTC GGGGCGAAA CTCTCAAGGA TCTTACCGCT GTTGAGATCC AGTTCGATGT AACCCACTCG TGCACCCCAAC
TTTTACAGG TAGTAACCTT TTGCAAGAAG CCCCCTTTT GAGAGTCTCT AGAATGGCGA CAACTCTAGG TCAAGCTACA TTGGGTGAGC ACGTGGGTG
4801 TGATCTTCAG CATCTTTTAC TTTCACCAAG GTTTCTGGT GAGCAAAAA GAGAAAGCAA AATGCCGCAA AAAAGGGAAT AAGGGCGACA CGGAAATGTT
ACTAGAAGTC GTAGAAAATG AAAGTGCTG CAAAGACCCA CTCGTTTTG TCCTTCCGTT TTACGGCGTT TTTTCCCTTA TTCCCGCTGT GCCTTTACAA
4901 GAATACTCAT ACTCTTCTT TTTCAATATT ATTGAAGCAT TTATCAGGGT TATTGCTCA TGAGCGGATA CATATTGAA TGTATTTAGA AAAATAAACA
CTTATGAGTA TGAGAAGGA AAAGTTATAA TAACTTCGTA AATAGTCCCA AATACAGAT ACTCGCCTAT GTATAAACTT ACATAAATCT TTTTATTGT
5001 AATAGGGGT CCGCGACAT TTCCCCGAAA AGTGCCACCT GACGTCTAAG AAACCAATTAT TATCATGACA TTAACCTATA AAAATAGGCG TATCACGAGG
TTATCCCCAA GCGCGTGTA AAGGGCTTT TCACGGTGGA CTGAGATTC TTTGGTAATA ATAGTACTGT AATTGGATAT TTTTATCCGC ATAGTCTCC
5101 CCCTTTCGTC TTCAA
GGAAAGCAG AAGTT

FIG. 3D



IGF-1 KIRA in Human MCF-7 Cells
Comparison of IGF-1 and Mutant IGF-1

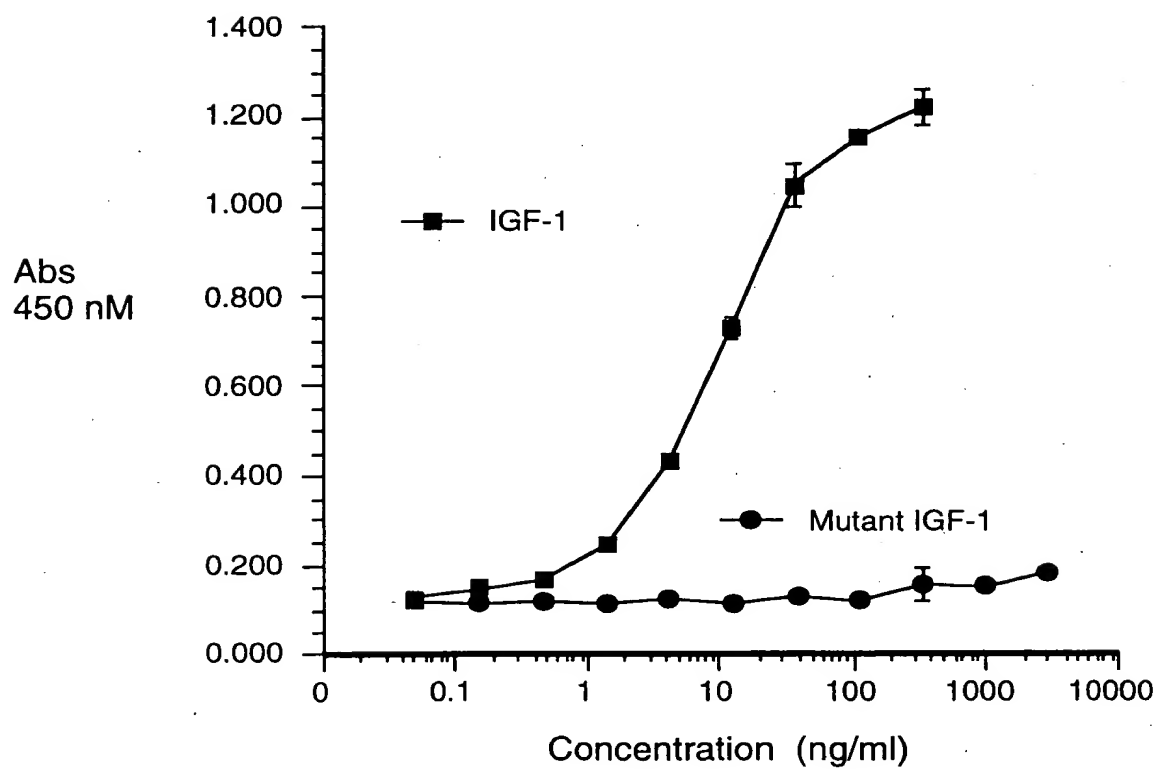
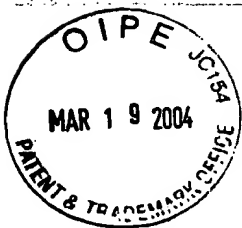


FIG. 4



IGF-1 (Leu²⁴ Ala³¹) is Inactive In Vitro

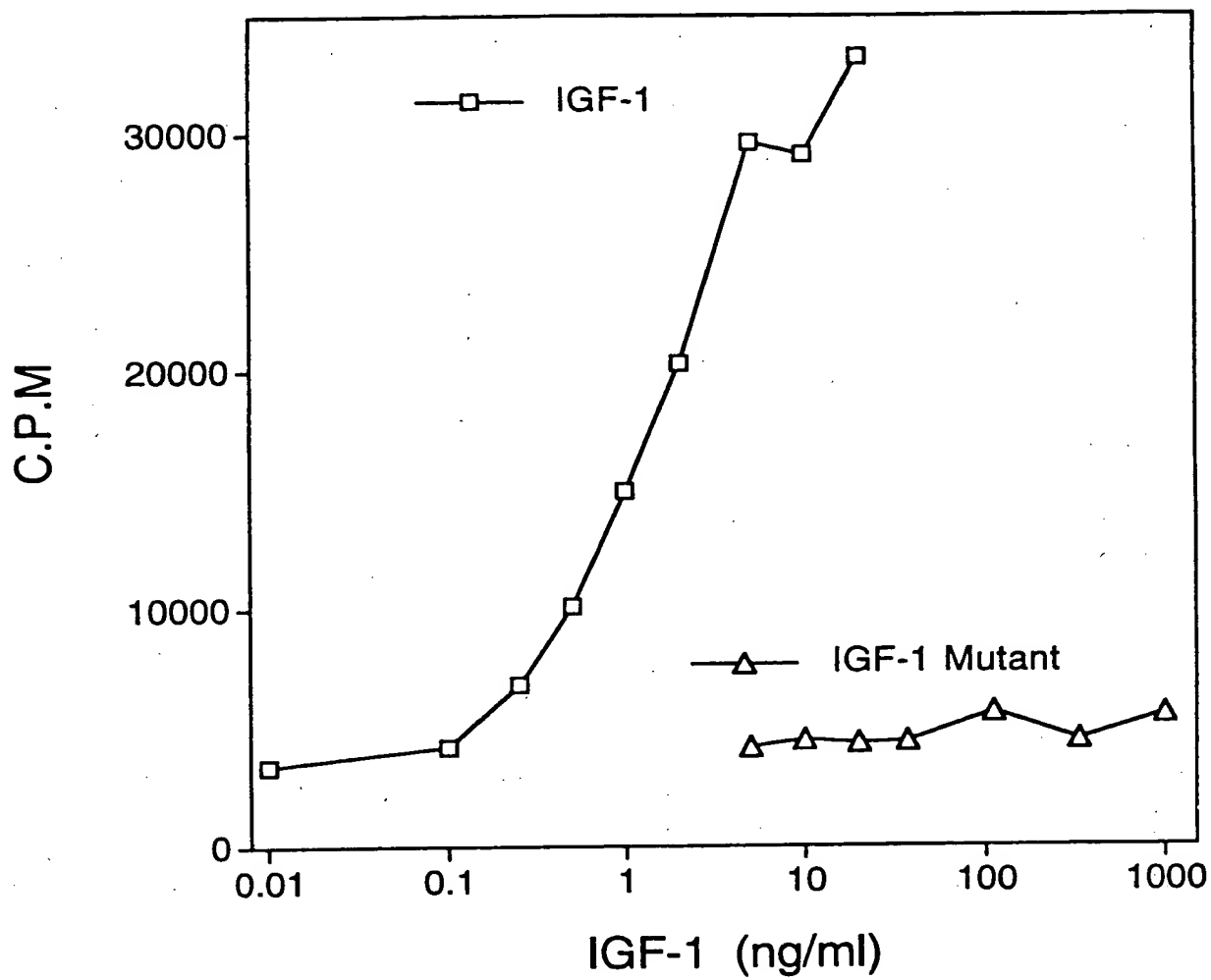


FIG. 5

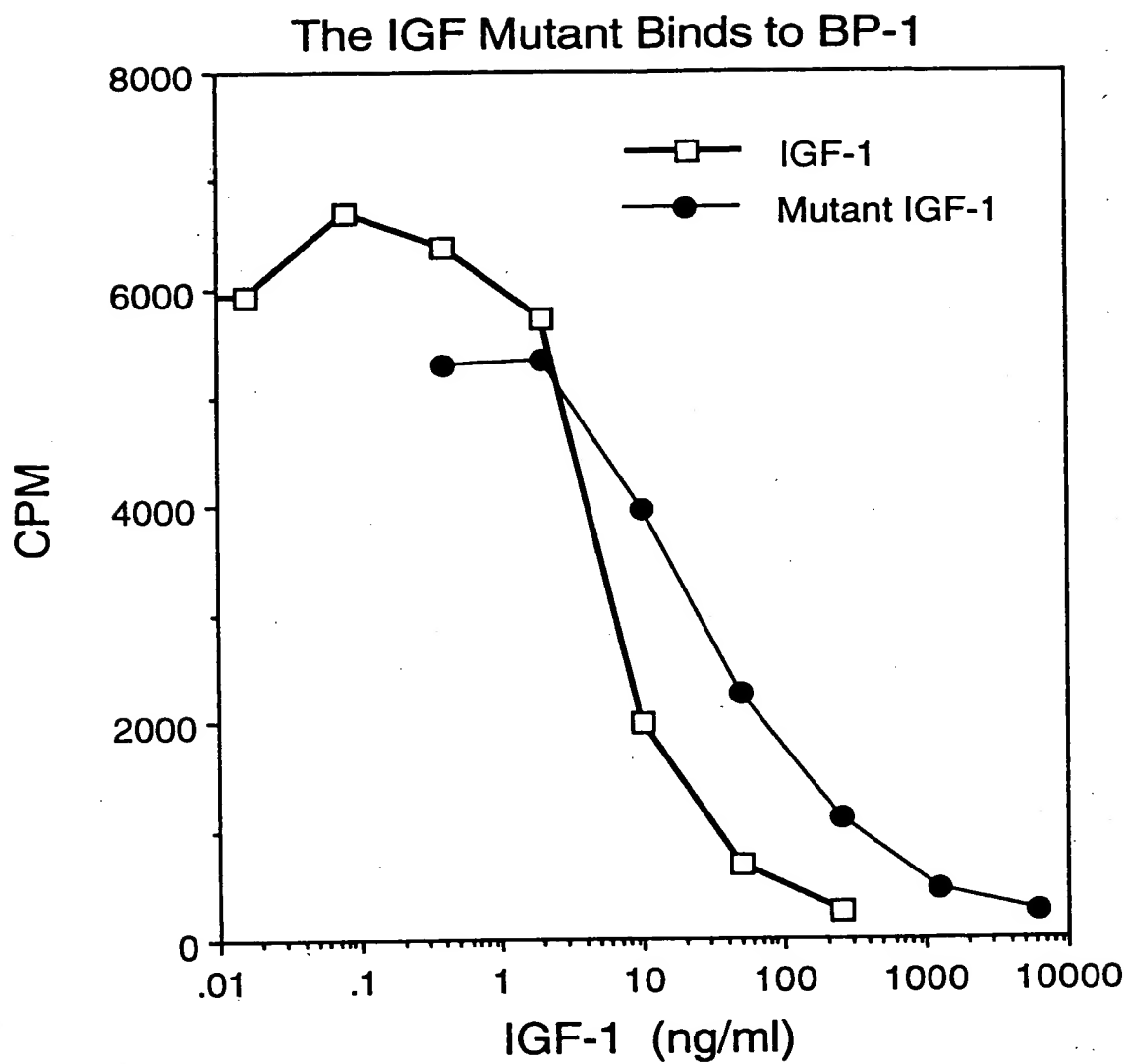
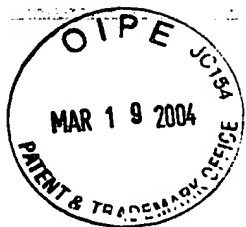


FIG. 6

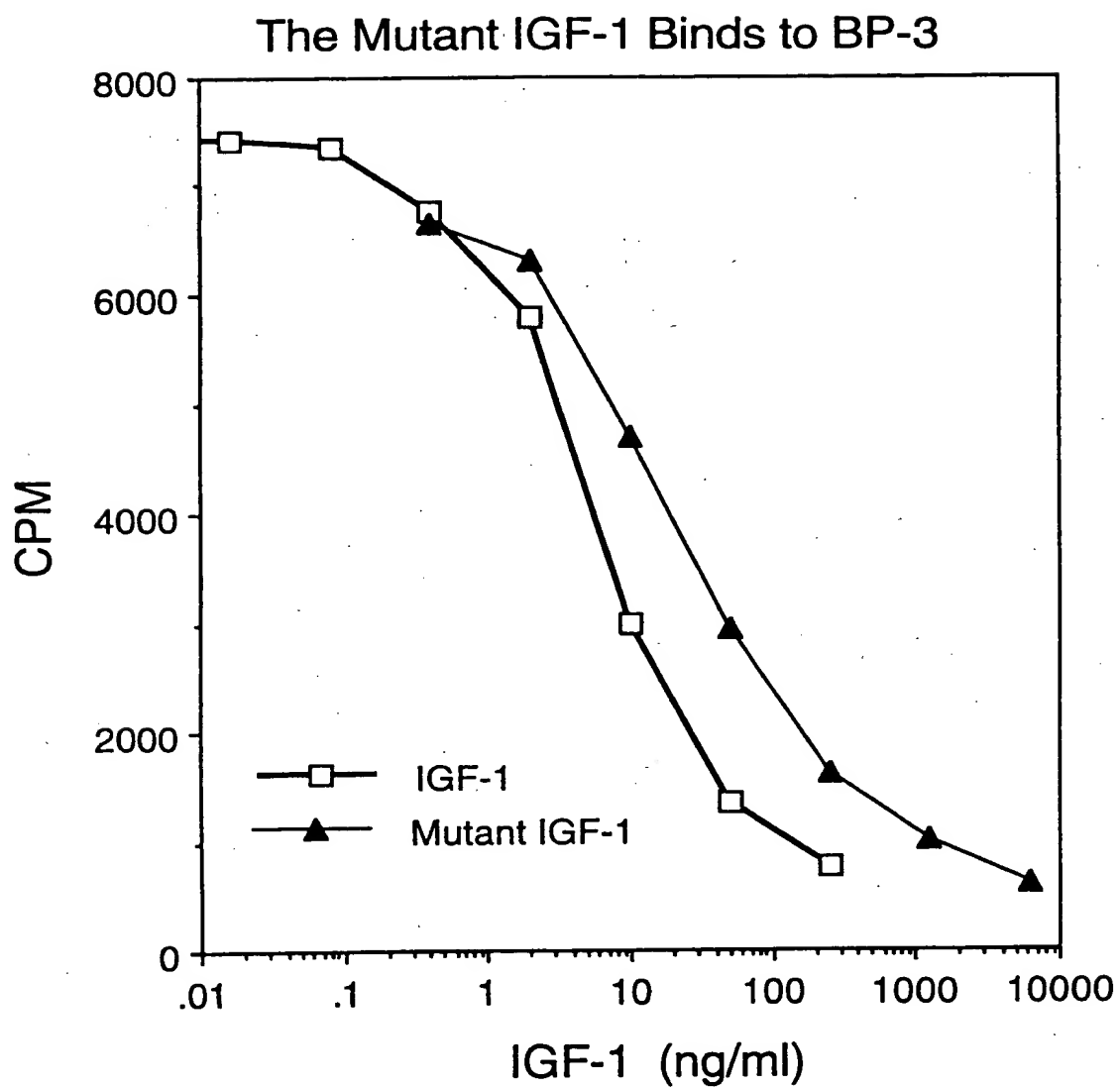
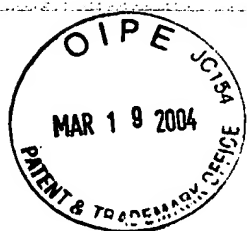


FIG. 7

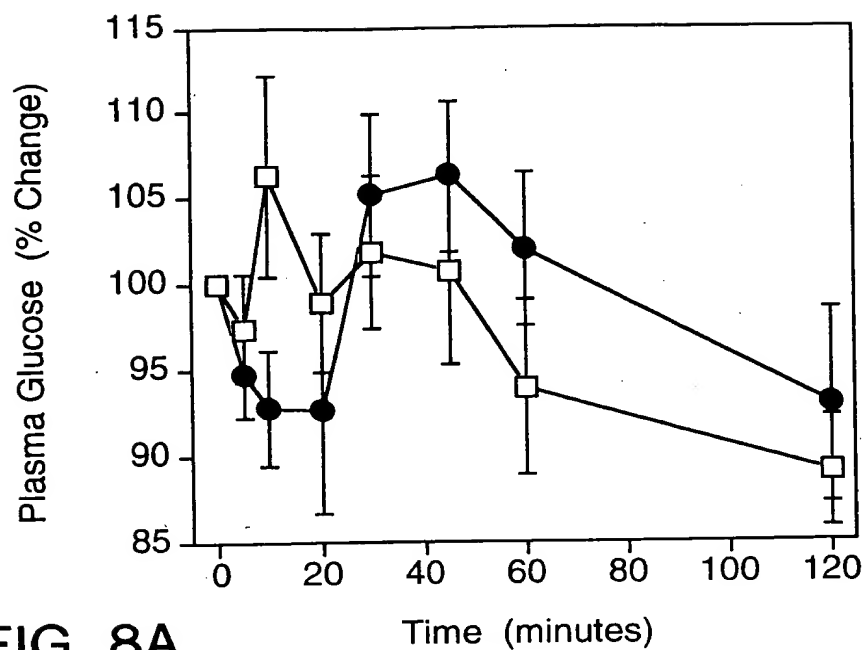
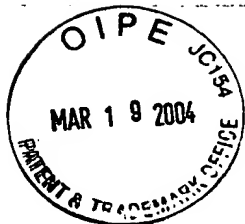


FIG. 8A

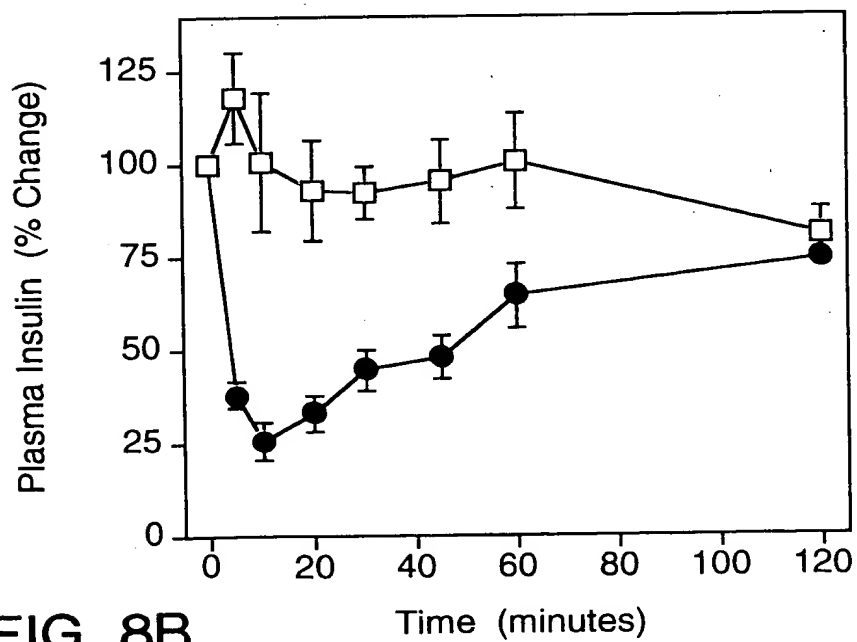


FIG. 8B

—□— Control —●— IGF-Mutant

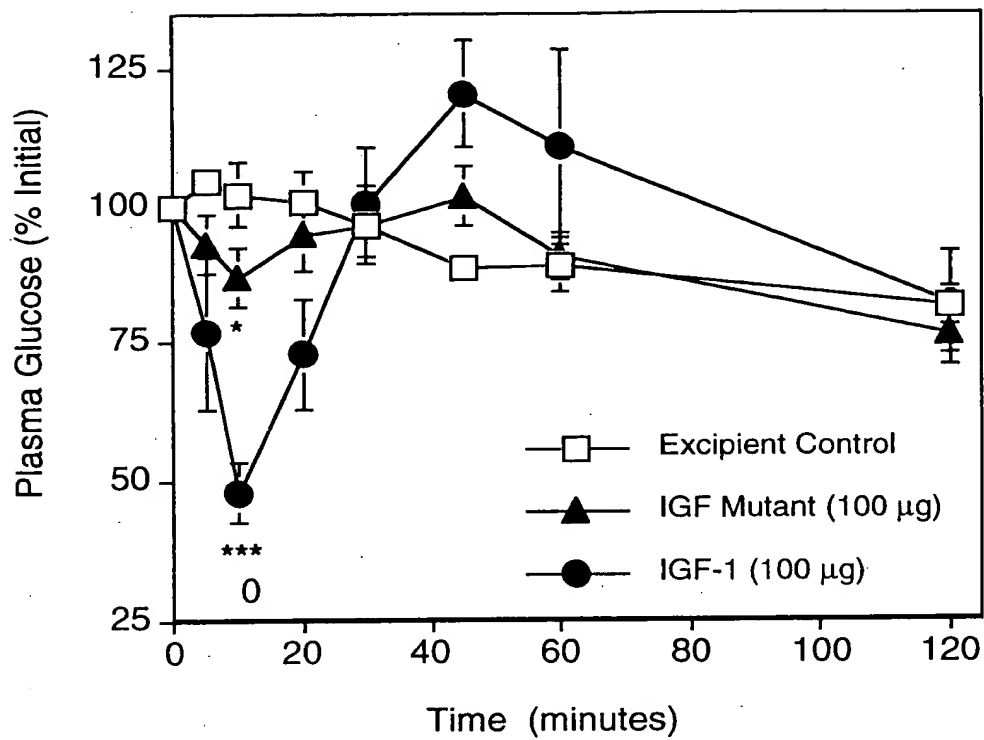


FIG. 9A

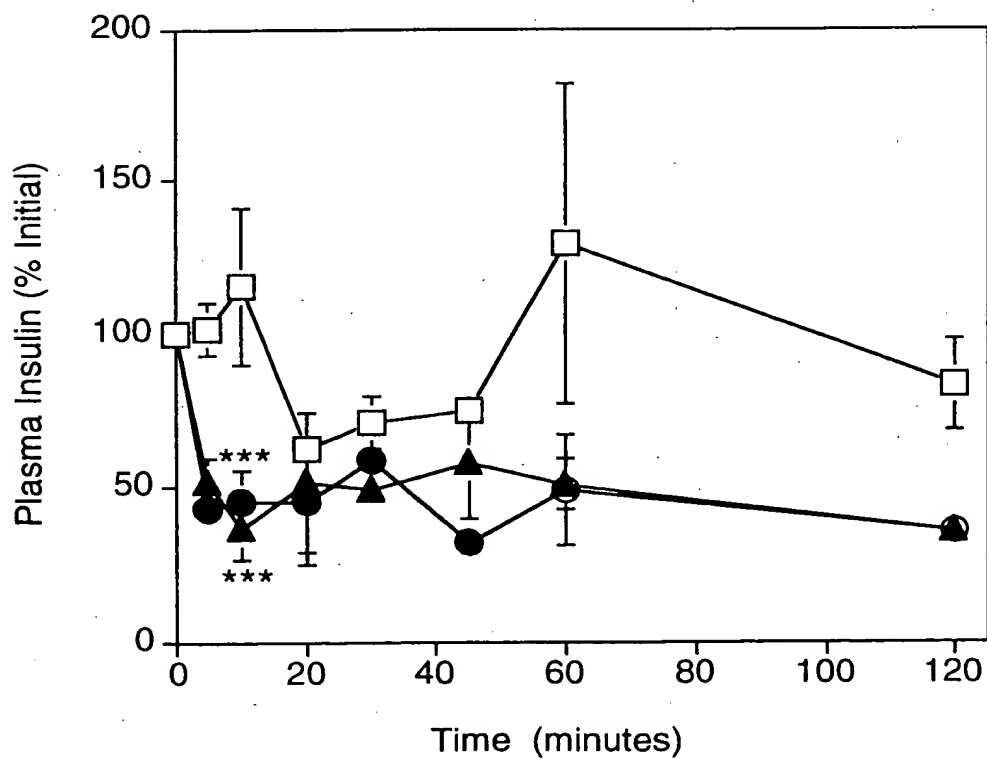


FIG. 9B

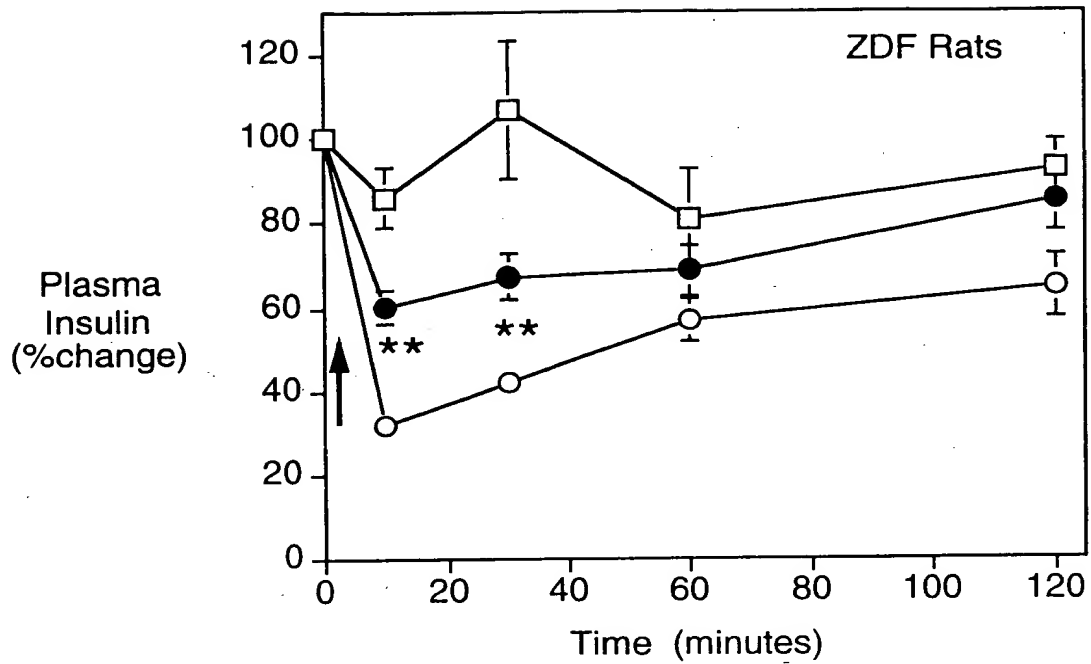


FIG. 10A

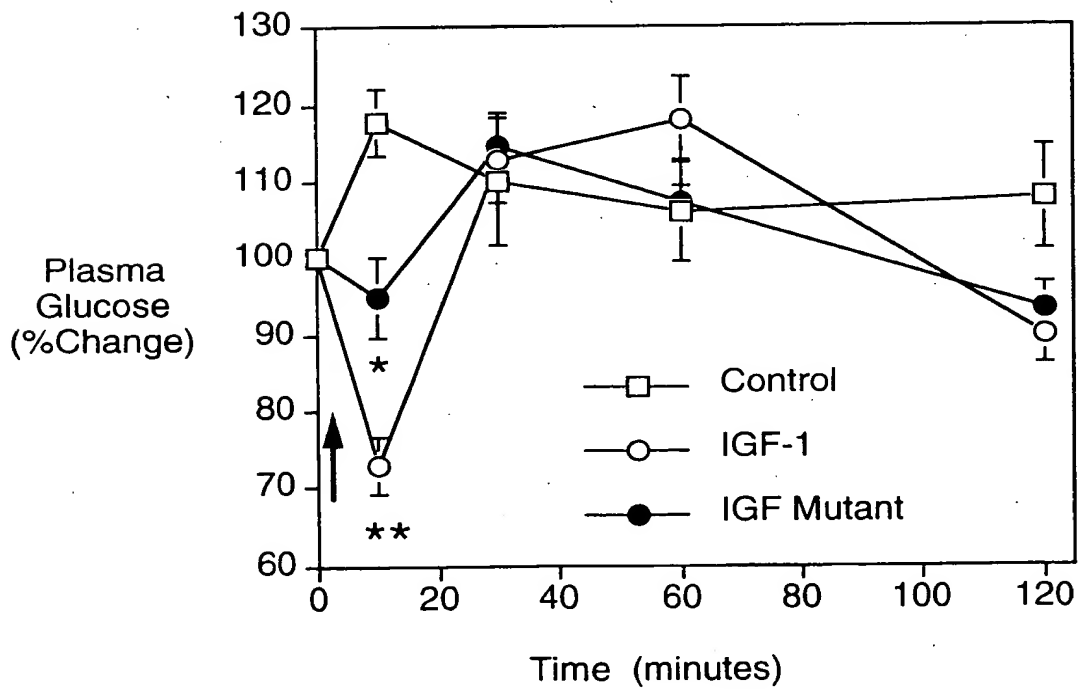


FIG. 10B

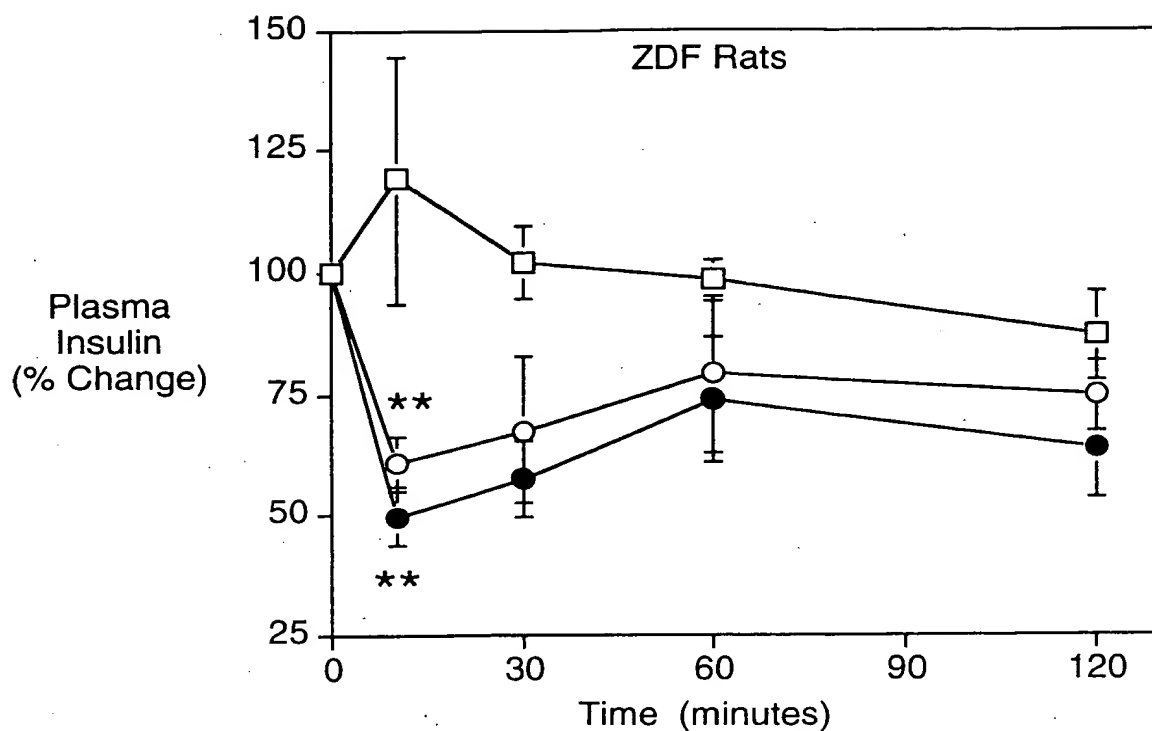


FIG. 11A

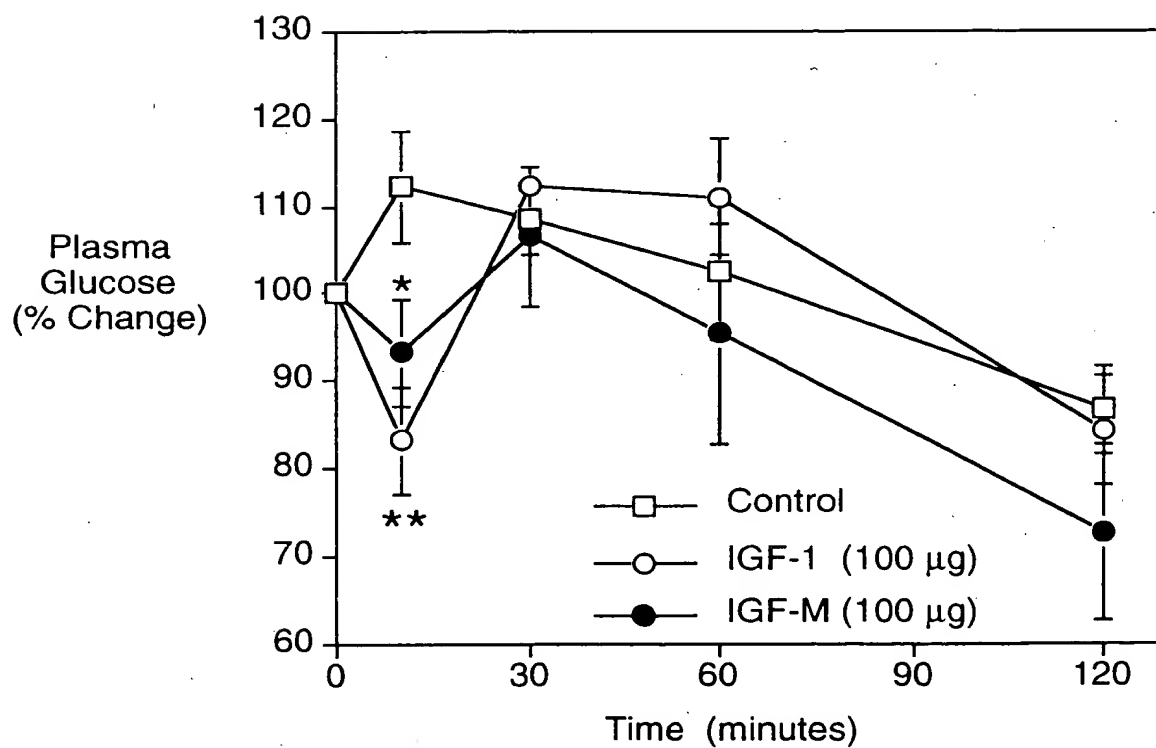


FIG. 11B

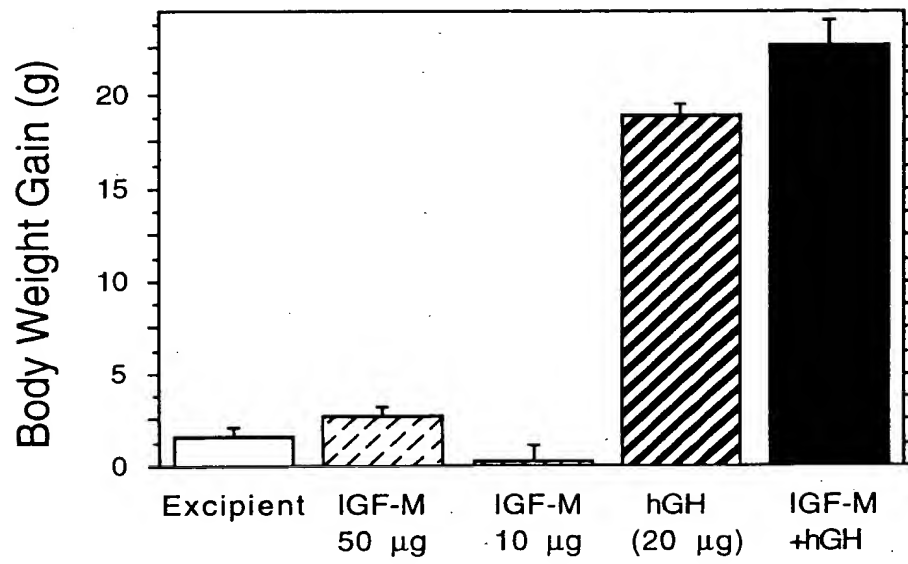


FIG. 12

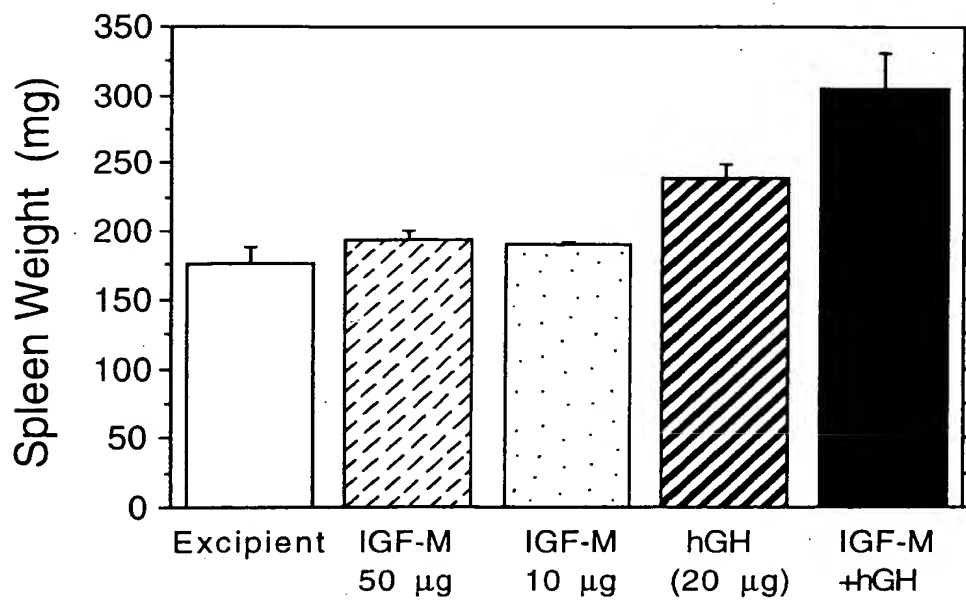


FIG. 13A

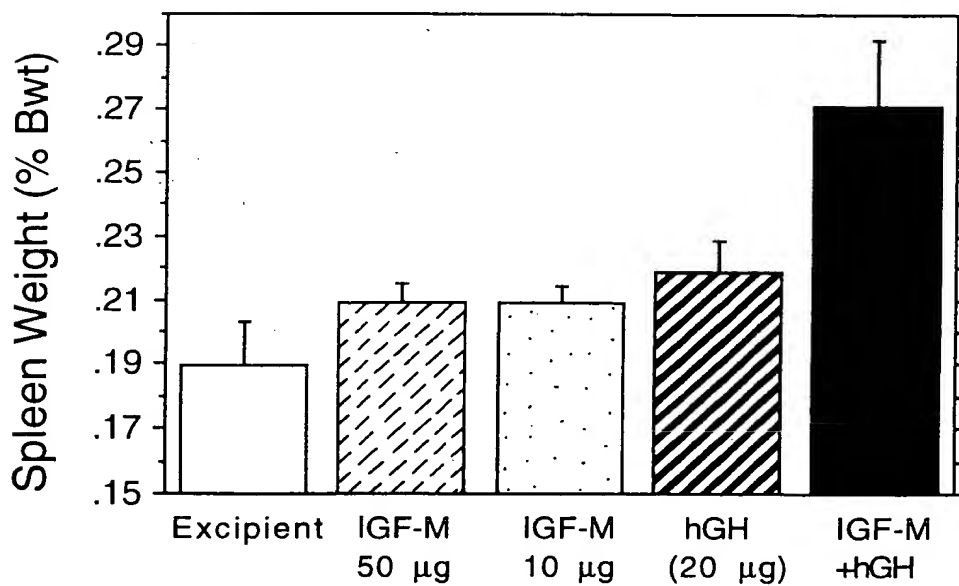


FIG. 13B

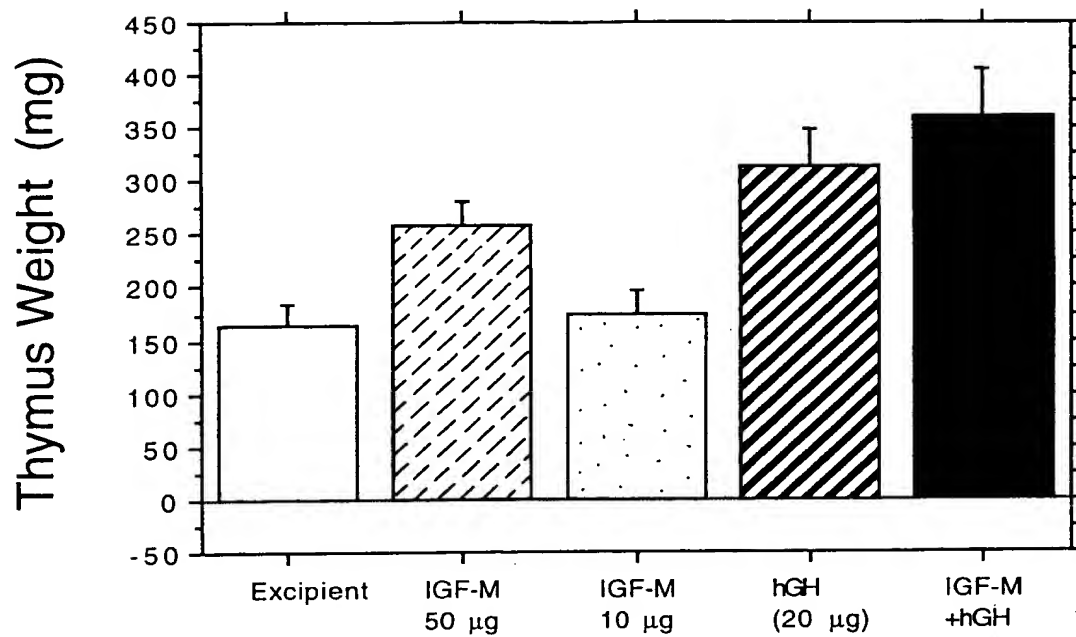


FIG. 14A

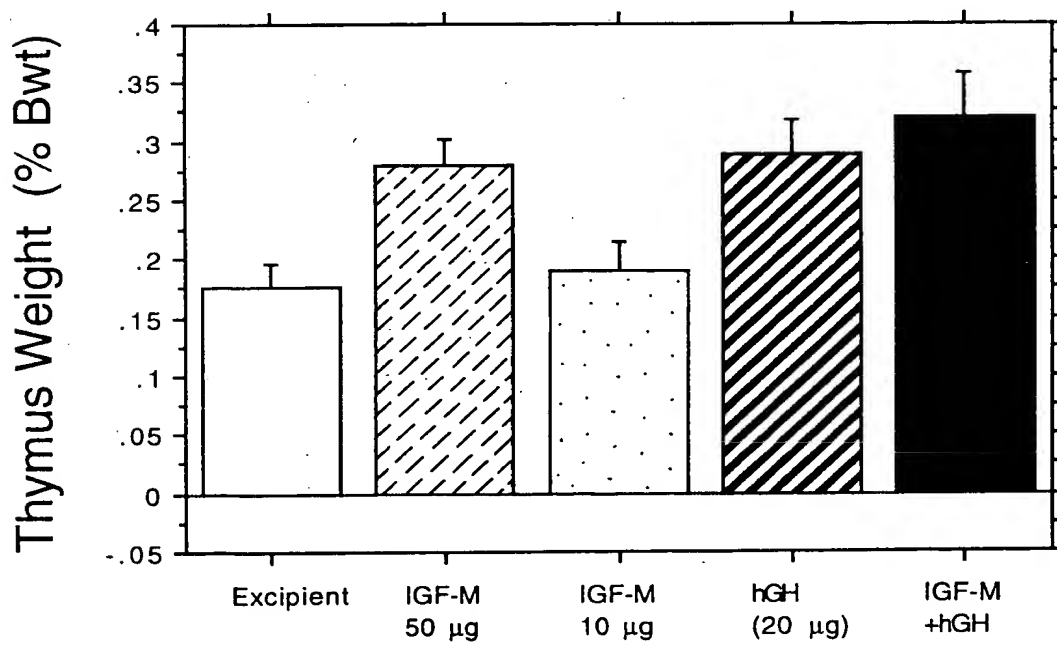


FIG. 14B

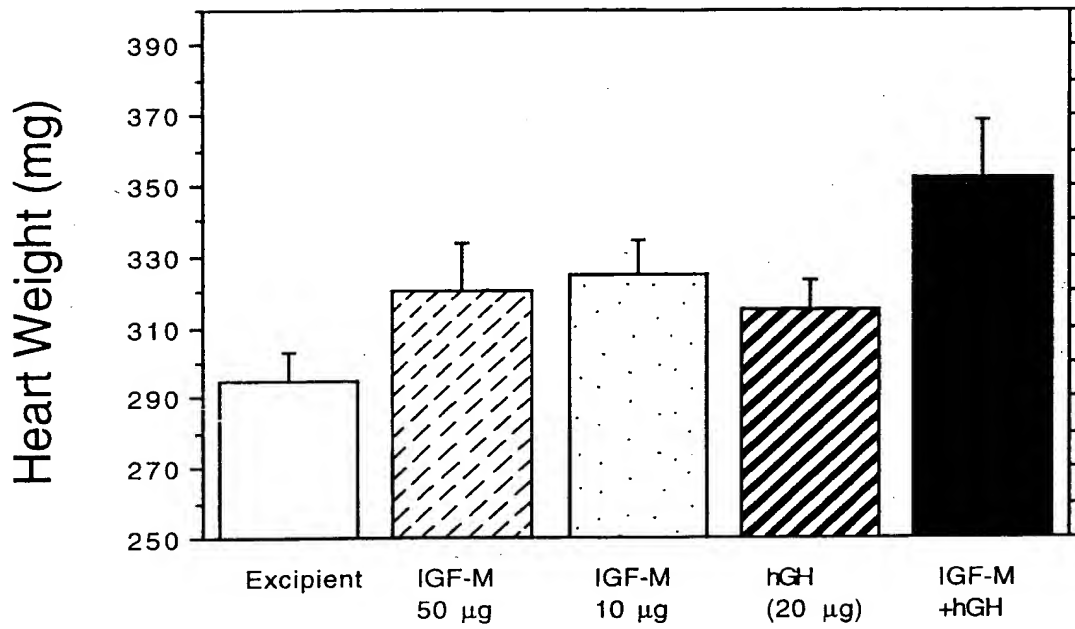


FIG. 15A

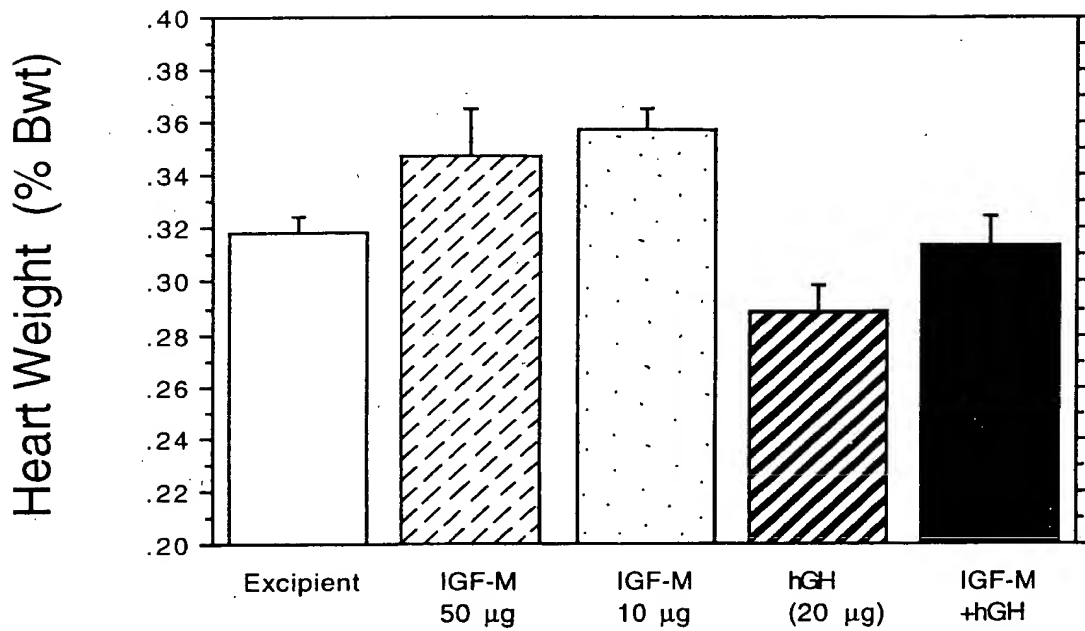


FIG. 15B

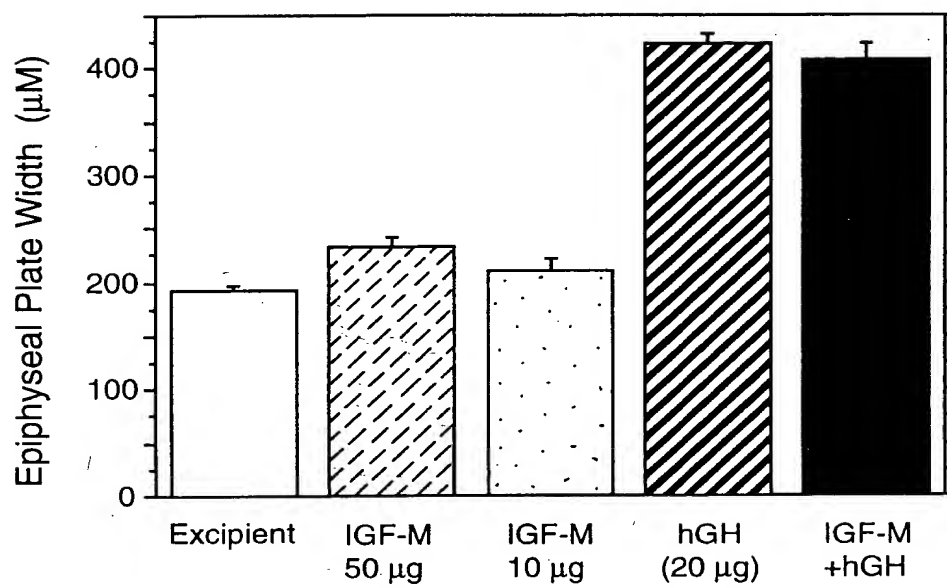


FIG. 16

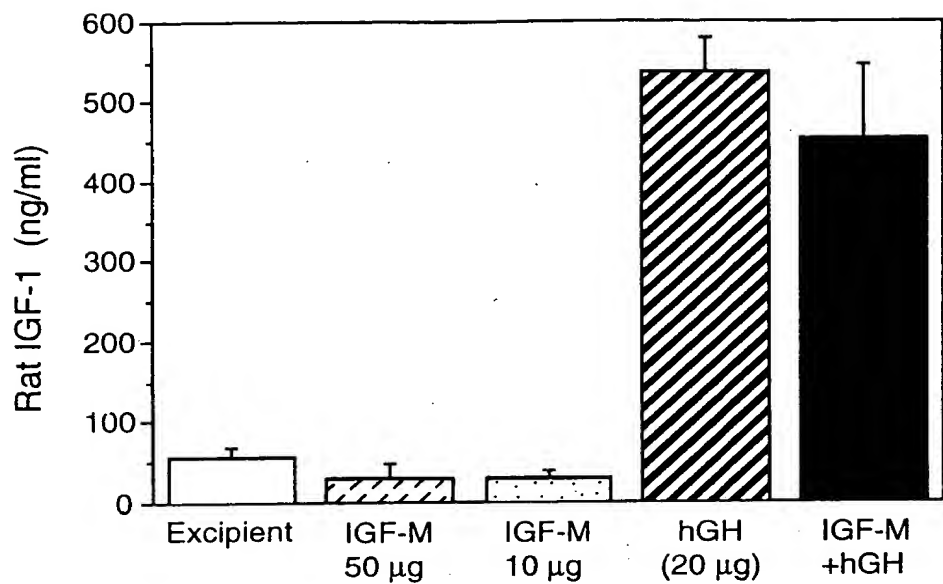


FIG. 17A

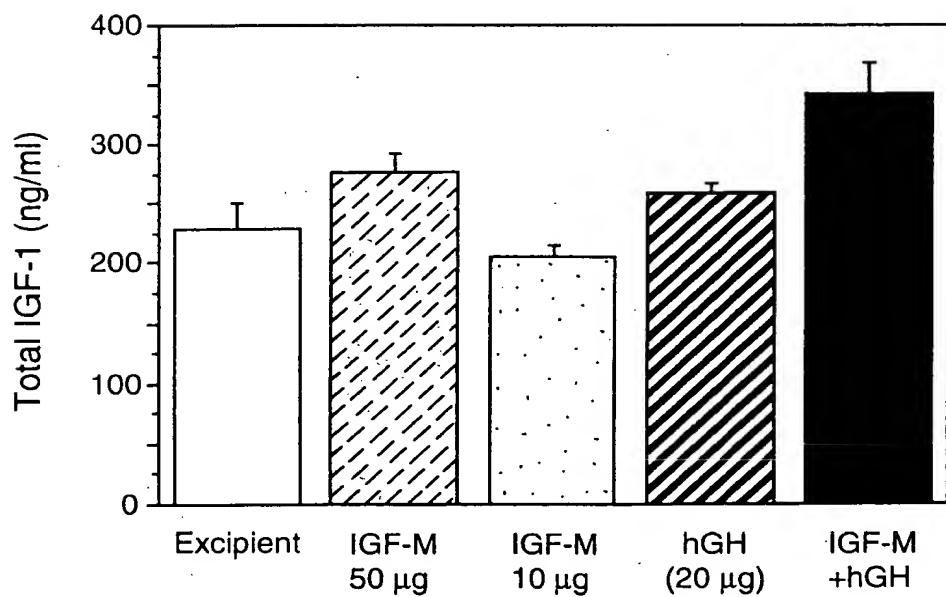


FIG. 17B

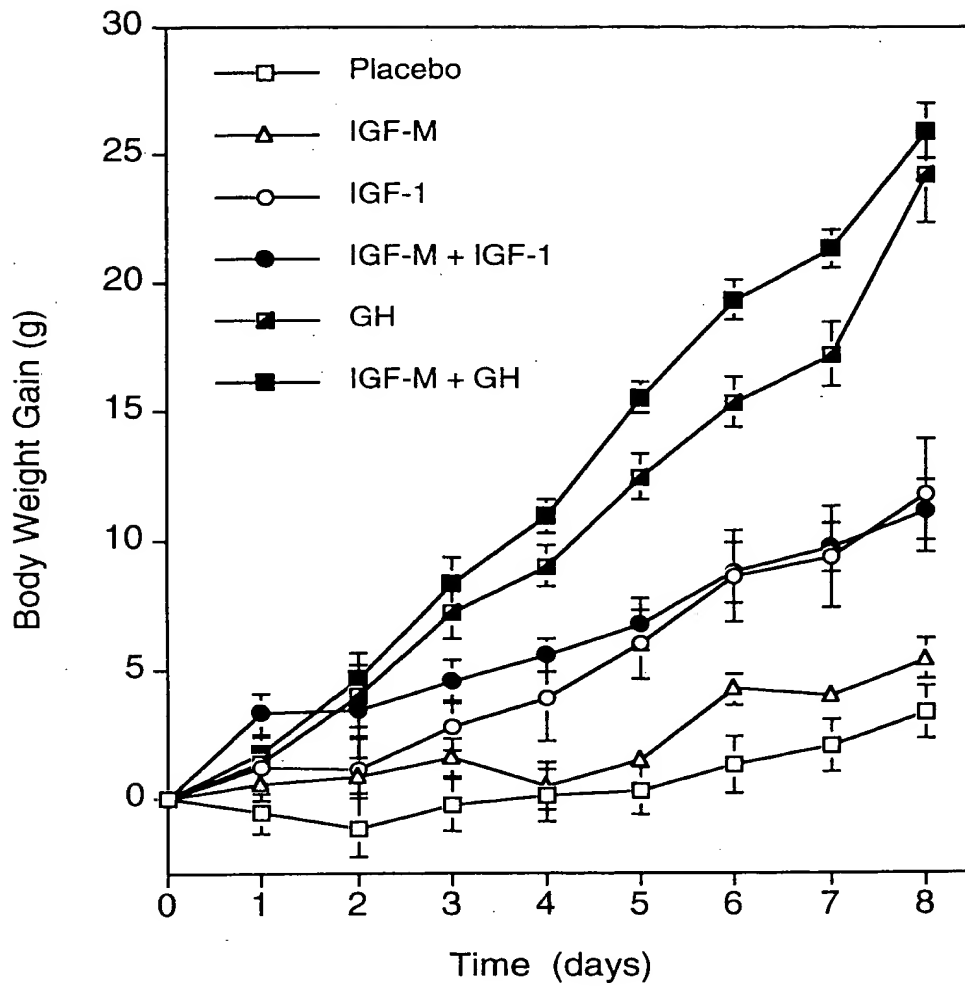


FIG. 18

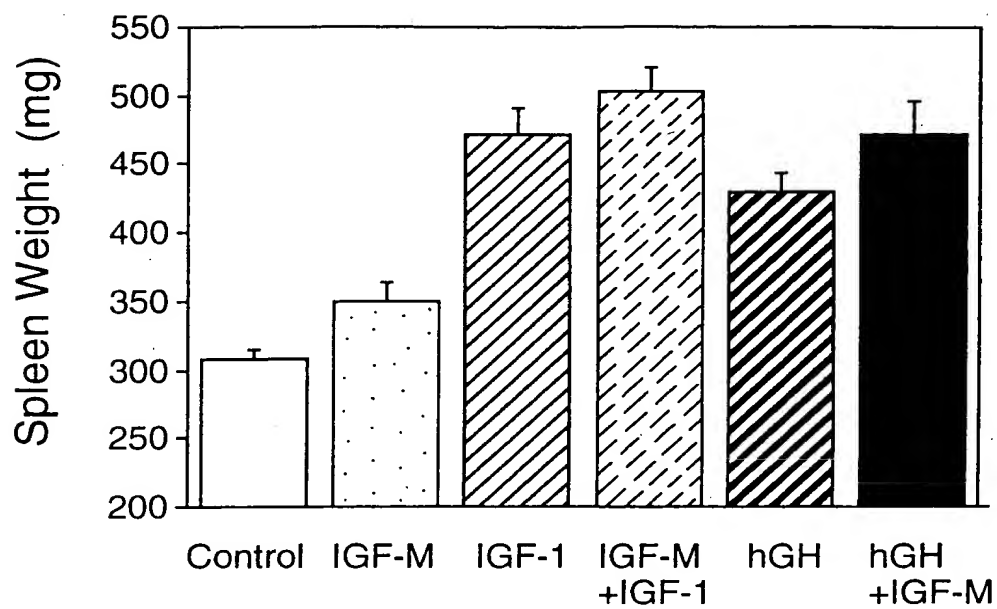


FIG. 19A

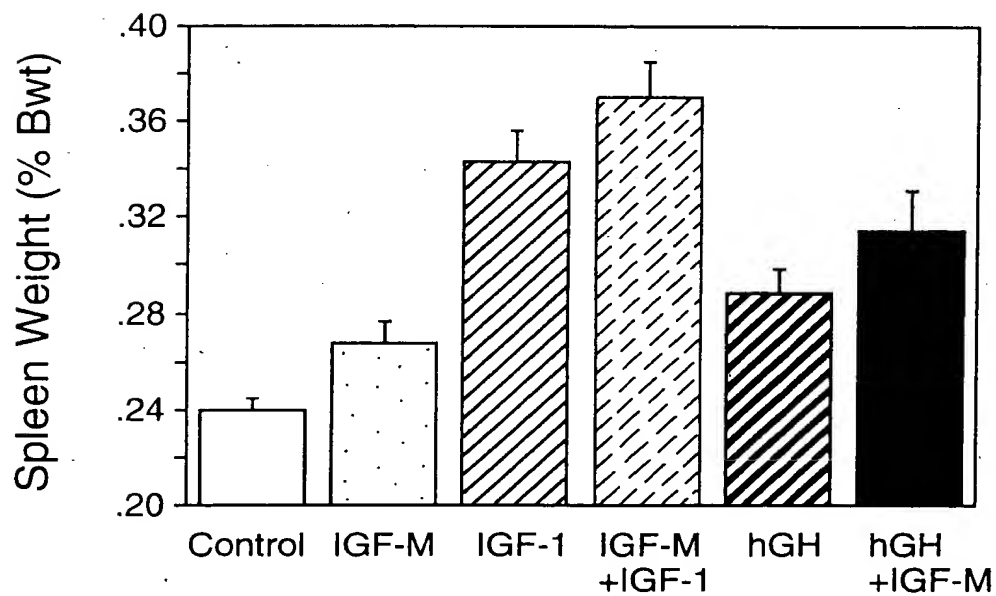


FIG. 19B

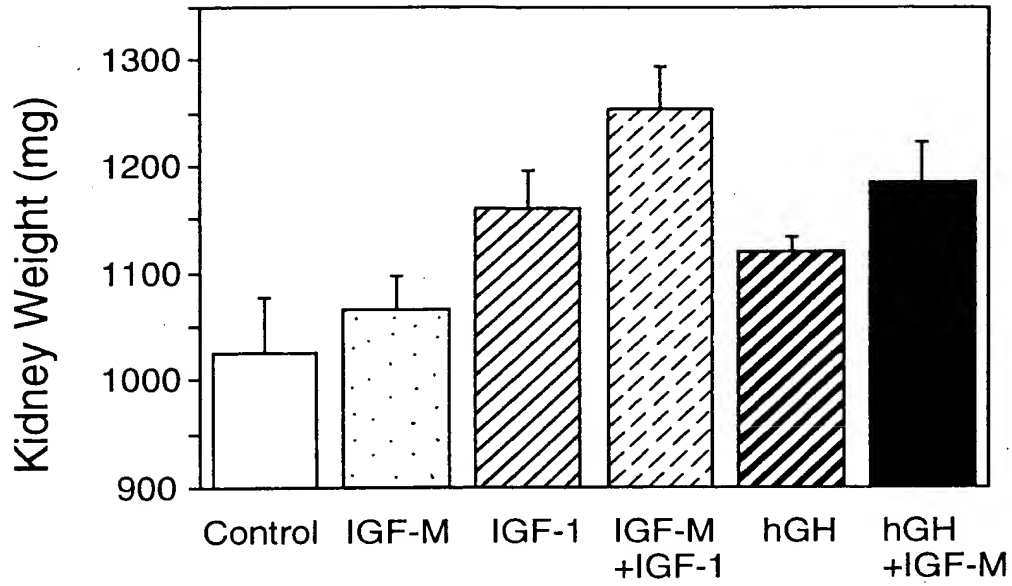


FIG. 20A

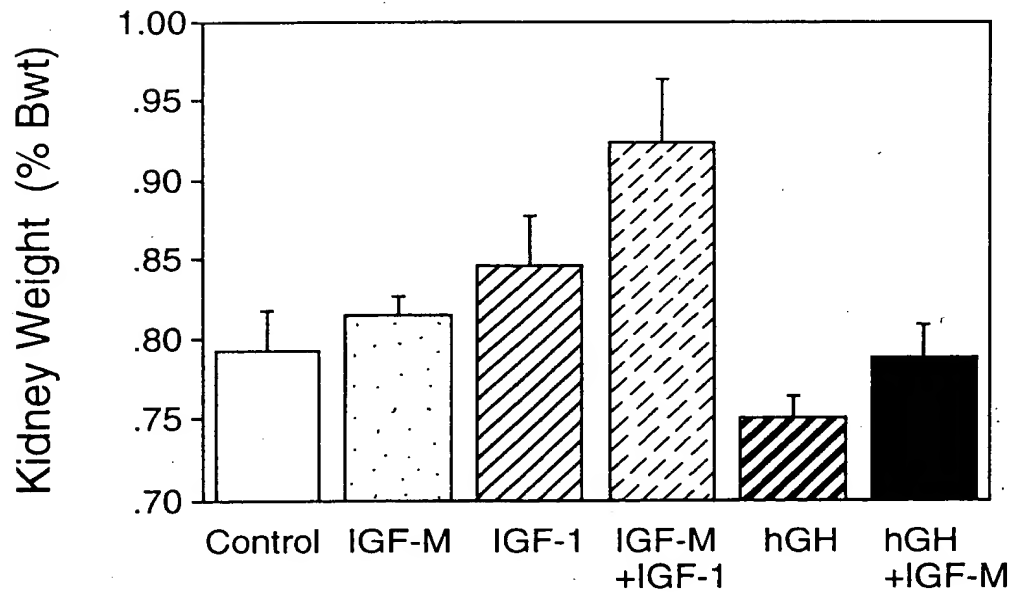


FIG. 20B

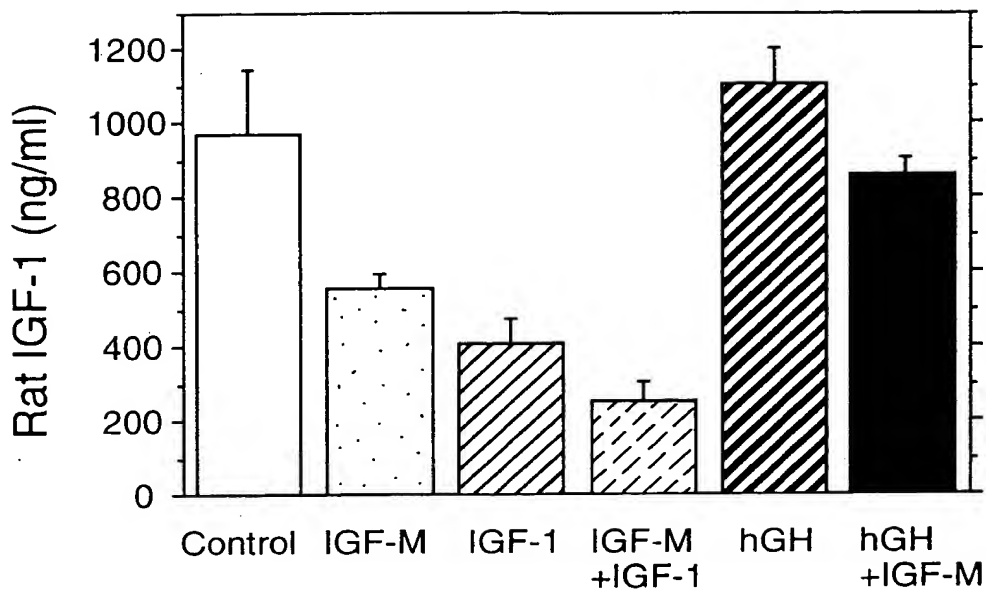


FIG. 21A

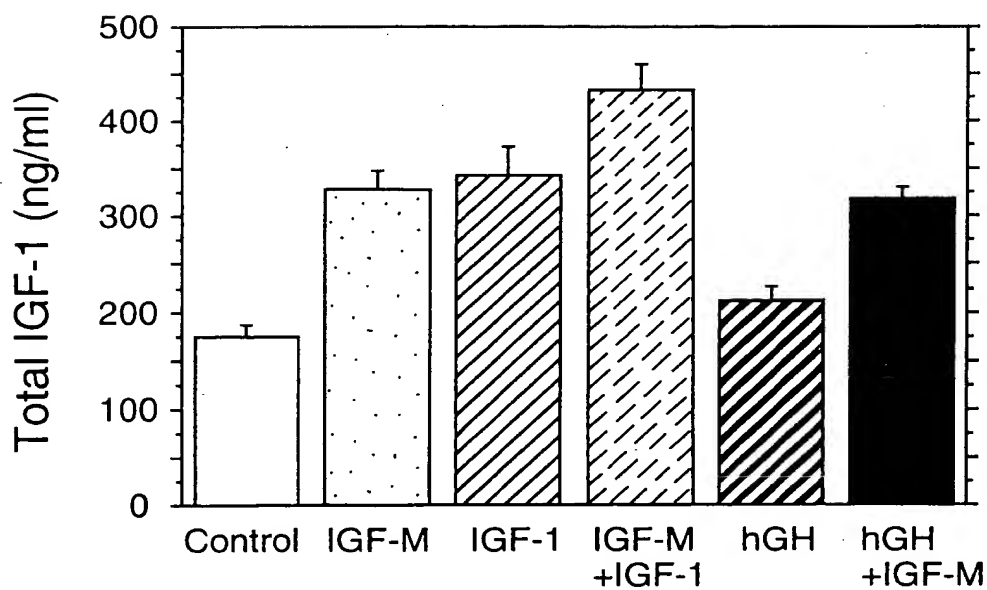


FIG. 21B

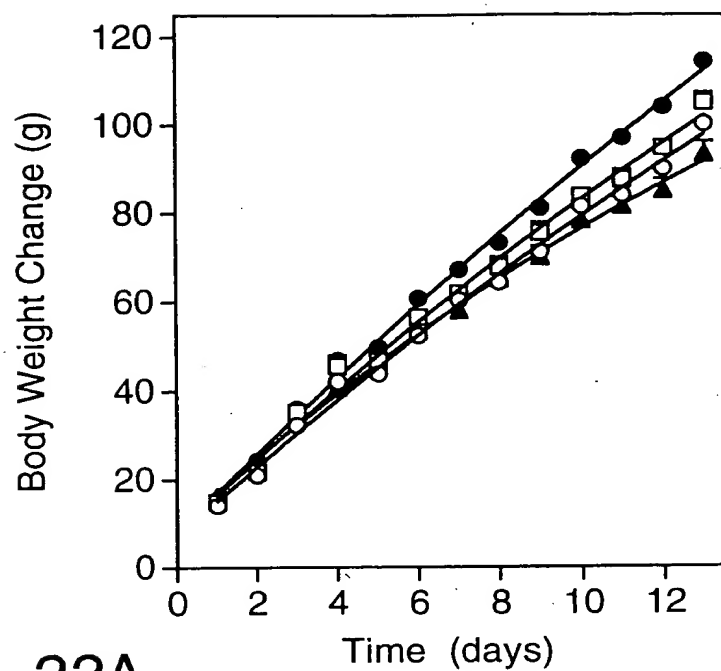


FIG. 22A

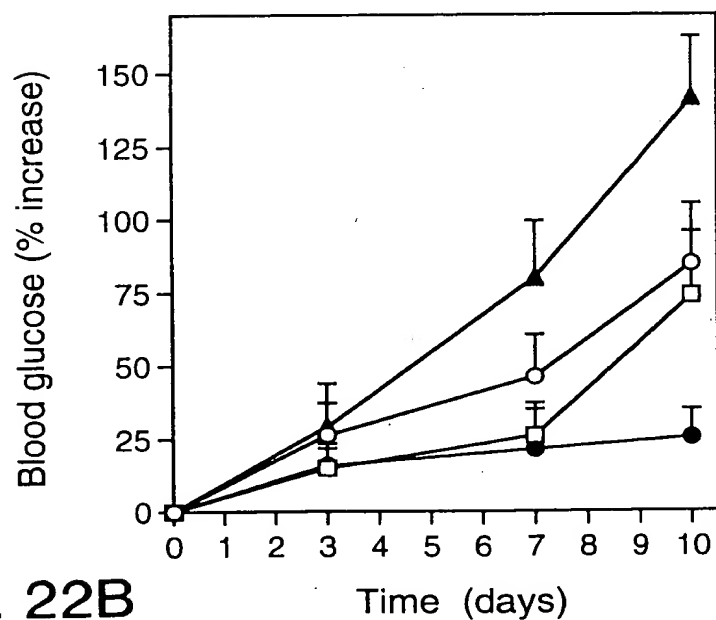
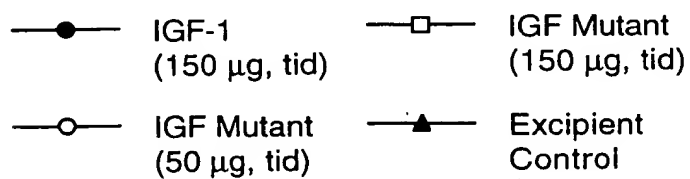


FIG. 22B



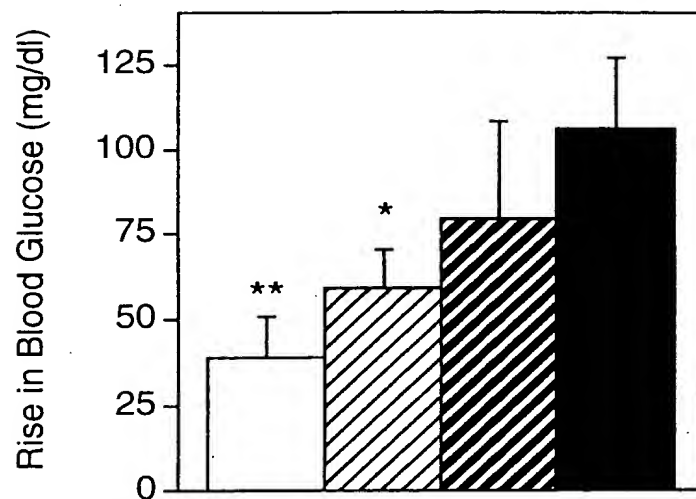


FIG. 23A

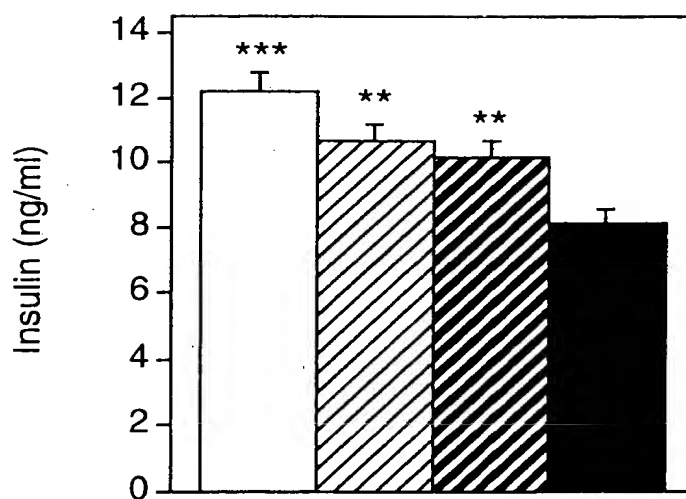
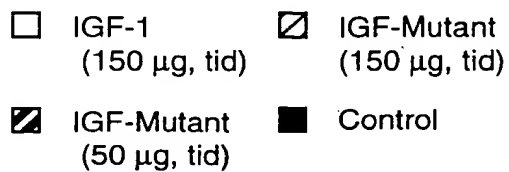


FIG. 23B



plasmid t4.g8
length: 5140 (circular)

1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTATATGCTG TACTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTCTCT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGGTACGA AGCGTTATAC CGCGTTTAC TGGTTGTGCG CAACTAACTA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA
CCCCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGAGC CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCACAA GCTGTCATAA AGTTGTCACG GCCGAGACTT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTTGTAACTA GTACGCAAGT
TTTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA AAAAAATAA AAAATTACAT AAACATTGAT CATCGGTTCA

401 TCACGTAAAA AGGGTATCTA GAGGTTGAGG TGATTTTATG AAAAAGATAA TCGCATTTCT TCTTGCACT ATGTTGCTTT TTTCTATTGC TACAAATGCC
AGTGCAATTT TCCCATAGAT CTCCAACCTC ACTAAATAC TTTTCTCTAT AGCGTAAAGA AGAACGTAGA TACAAGCAAA AAAGATAACG ATGTTTACGG

501 TATGCATCTG GTACCGCCAT GGCTGATCCG AACCGTTTCC GCGGTAAAGA TCTGGCAGGT TCACCAGGTG GAGGATCCGG AGGAGCGCC GAGGGTGACG
ATACGTAGAC CATGGCGGTA CCGACTAGGC TTGGCAAAGG CGCCATTTCT AGACCGTCCA AGTGGTCCAC CTCCTAGGCC TCCTCCGCGG CTCCCACTGC

1 SerG lyThrAlaMe tAlaAspPro AsnArgPheA rgGlyLysAs pLeuAlaGly SerProGlyG lyGlySerG lYglyGlyAla GluGlyAspAsp

33 ProAlaLy salaAlaPhe AsnSerLeug lnaLaSerAl aThrGluTyr ileGlyTyrA laTrpAlaMe tValValVal ileValGlyA laThrIleGly

601 ATCCCGCAAA AGCGGCCTTT AACTCCCTGC AAGCCTCAGC GACCGAATAT ATCGGTTATG CGTGGGCGAT GGTGTTGTGTC ATTGTCGGCG CAACATATCGG
TAGGGCGTTT TCGCCGGAAA TTGAGGGAGC TTGAGGAGTCG CTGGCTTATA TAGCCAATAC GCACCCGCTA CCAACAACAG TAACAGCCGC GTTGATAGCC

701 TATCAAGCTG TTTAAGAAAT TCACCTCGAA AGCAAGCTGA TAAACCGATA CAATTAAAGG CTCCTTTTGG AGCCTTTTIT TTTGGAGATT TTCAACGTGA
ATAGTTCGAC AAATTCTTTA AGTGGAGCTT TCGTTCGACT ATTTGGCTAT GTTAATTTC GAGGAAAAACC TCGGAAAAAA AAACCTCTAA AAGTTGCACT

66 ileLysLeu PheLysLysP heThrSerLy salaSer

801 AAAAATTATT ATTGCAATT CCTTTAGTTG TTCTCTACTC GCTGAAACTG TTGAAAGTTG TTTAGCAAAA CCCCATACAG AAAATTCAAT
TTTTTAATAA TAAGCGTTAA GGAATCAAC AAGGAAAGAT AAGAGTGAGG CGACTTGAC AACTTTCAAC AAATCGTTT GGGGTATGTC TTTTAAGTAA

901 TACTAACGTC TGGAAAGACG ACAAACCTT AGATCGTTAC GCTAACTATG AGGTTGTCT GTGGAATGCT ACAGCGGTG TAGTTGTAC TGGTGACGAA
ATGATTGCAG ACCTTCTGC TGTTTTGAAA TCTAGCAATG CGATTGATAC TCCCAACAGA CACCTTACGA TGTCGCAAC ATCAAAACATG ACCACTGCTT

1001 ACTCAGTGC TAGCTAGAT GGGGTGGCT CTGGTCCGG TGATTTTGTAT TATGAAAAGA TGGCAACCG TAATAAGGG GCTATGACCG AAAATGCCGA
TGAGTCACAG ATCGATCTCA CCGCCACCGA GACCAAGGCC ACTAAACTA ATACTTTCT ACCGTTTGGG ATTTATTTCCC CGATCTGGC TTTTACGGCT

FIG. 24A





1101 TGAAAAACGG CTACAGTCTG ACGCTAAAGG CAAACTTTGAT TCTGTCGCTA CTGATTACGG TGCTGCTATC GATGGTTTCA TTGGTGACGT TTCCGGCCTT
ACTTTTGGCG GATGTCAGAC TGGGATTTC GTTTGAAC TAAGAGCGAT GACTAATGCC ACGACGATAG CTACCAAGT AACCACTGCA AAGCCGGAA

1201 GCTAATGGTA ATGGTGCTAC TGGTGATTTT GCTGGCTCTA ATTCCCAAT GGCTCAAGTC GGTGACGGTG ATAAATTCACC TTAAATGAAT AATTCCGTC
CGATTACCAT TACCACGATG ACCACTAAAA CGACCGAGAT TAAGGGTTTA CCGAGTTTCA CCACTGCCAC TATTAAGTGG AAATTACTTA TTAAAGGCAG

1301 AATATTATCC TTCCCTCCCT CAATCGGTTG AATGTCGCCC TTTTGTCTTT AGCGTGGTA AACCATATGA ATTTTCTATT GATTGTGACA AAATAAACTT
TTATAAATGG AAGGGAGGA GTTAGCCAC GTTAGCCAC AAAACAGAAA TCGCGACCAT TTGGTATACT TAAAAAGATAA CTAACACTGT TTTATTGAA

1401 ATTCCGTGGT GTCTTTTGGT TTTCTTTTATA TGTGTCAC TTTTGTCTAC GTTTGTCTAAC ATACTGCGTA ATAAGGAGTC TTAATCATGC
TAAGGCACCA CAGAAACGCA AAGAAATAT ACAACGGTGG AAATACATAC ATAAAGATG CAAACGATTG TATGACGCAT TATTCCTCAG AATTAGTACG

3201 ACTCAAAGGC GGTAAATACGG TTATCCACAG AATCAGGGGA TAACGCAGGA AAGAACATGT GAGCAAAAGG CCAGCAAAAG GCCAGGAACC GTAAAAAGGC
TGAGTTTCCG CCATTATGCC AATAGGTGTC TTAGTCCCTT ATGCGTCCCT TTTTGTGACA CTCGTTTTCC GGTGCTTTGG CATTTTCCG

3301 CGCGTTGCTG GCGTTTTC ATAGGCTCCG CCCCCCTGAC GAGCATCACA AAAATCGACG CTCAAAGTCAG AGGTGGCGAA ACCCGACAGG ACTATAAAGA
GCGCAACGAC CGCAAAAAGG TATCCGAGGC GGGGGGACTG CTCGTAGTGT TTTTAGCTGC GAGTTCAGTC TCCACCGCTT TGGGCTGTCC TGATATTCT

3401 TACCAGGCGT TTCCCTCTGG AAGCTCCCTC GTGGCTCTC CTGTTCCGAC CCGTCCGCTT ACCGGATACC TGTCGCGCTT TCTCCCTTCG GGAAGCGTGG
ATGTTCCGCA AAGGGGACG TTCGAGGGAG CACGCGAGAG GACAAGGCTG GAGCGGCGAA TGGCCTATGG ACAGGCGGAA AGAGGGAAGC CCTTCGCACC

3501 CGCTTTCTCA TAGTCAAGC TGTAAGTATC TCAGTTCCGT GTAGGTCGTT CGTCCCAAGC TGGGCTGTGT GCAGCAACCC CCGTTTCAGC CCGACCGCTG
GGGAAAGAGT ATCAGTGGG ACATCCATAG AGTCAAGCCA CATCCAGCAA GCGAGGTTTC ACCCGACACA CGTGTTCGGG GGGCAAGTCG GGTGGCGGAC

3601 CGCCTTATCC GGTAACTATC GTCTTGAGTC CAACCCGGTA AGACACGACT TATCGCCACT GGCAGCAGCC ACTGGTAACA GGATTAGCAG AGCGAGGTAT
GCGGAATAGG CCATTGATAG CAGAACTCAG GTTGGGCCAT TCTGTGCTGA ATAGCGGTGA CCGTCGTCGG TGACCATGT CCTAATCGTC TCGCTCCATA

3701 GTAGGCGGTG CTACAGAGTT CTTGAAGTGG TGSCCTAACT ACGGCTACAC TAGAAGGACA GTATTGTTGTA TCTGCGCTCT GCTGAAGCCA GTTACCTTCG
CATCCGCCAC GATGCTCAA GAACCTCACC ACCGGATTGA TGCCGATGTG ATCTTCCTGT CATAAACCAT AGACGCGAGA CGACTTCGGT CAATGGAAGC

3801 GAAAAAGAGT TGGTAGTCT TGATCCGGCA AACAAACCCAC CGCTGGTAGC GGTGGTTTTT TTGTTTGCAA GCAGCAGATT ACGCGCAGAA AAAAAGGATC
CTTTTCTCTA ACCATCGAGA ACTAGGCCGT TTGTTGGTG GCGACCATCG CCACCAAAAA AACAAACGTT CGTCGCTCTAA TGCGGCTCTT TTTTTCCTAG

3901 TCAAGAAGAT CCTTTGATCT TTTCTACGG GTCTGACGCT CAGTGGAAAG AAAACTCAGG TTAAGGGATT TTGGTCATGA GATTATCAA AAGGATCTTC
AGTCTTCTA GGAACTAGA AAAGATGCC CAGACTGCGA GTCACTTTC GTCACTTTC AATTCCCTAA AACCACTACT CTAATAGTTT TTCCTAGAAG

4001 ACCTAGATCC TTTTAAATTA AAAATGAAGT TTTAAATCAA TCTAAAGTAT ATATGAGTAA ACTTGGTCTG ACAGTTACCA ATGCTTAATC AGTGAGGCAC
TGGATCTAGG AAAATTAAAT TTTTACTTCA AAATTAGTT AGATTTCATA TATACTCATT TGAACCCAGC TGTCAATGGT TACGAATTAG TCACCTCGTG

FIG. 24B



4101 CTATCTCAGC GATCTGTCTA TTTCTGTTTCAT CCATAGTTGC CTGACTCCCC GTCTGTGTAGA TAACATAGAT ACGGAGGGC TTACCATCTG GCCCCAGTGC
GATAGAGTGC CTAGACAGAT AAGCAAGTA GGTATCAACG GACTGAGGG CAGCATCTCT ATTGATGCTA TGCCCTCCCG AATGGTAGAC CGGGGTACAG

4201 TGCAATGATA CCGCGAGACC CACGCTCACC GGCTCCAGAT TTATCAGCAA TAAACCAGCC AGCCGGAAGG GCCGAGCGCA GAAGTGGTCC TGCAACTTTA
ACGTTACTAT GCGCTCTGG GTGCGAGTGG CCGAGGTCTA AATAGTCTCTT ATTTGGTCCG TCGGCTTCC CGGCTCGCGT CTTACCCAGG ACGTTGAAAT

4301 TCCGCCCTCCA TCCAGTCTAT TAAATTGTTGC CCGGAAGCTA GAGTAAGTAG TTGCCCAGTT AATAGTTTGC GCAACGTTGT TGCCATTGCT GCAGGCATCG
AGGCGGAGGT AGGTCAGATA ATTAACACAG GCCCTTCGAT CTCAATTCATC AAGCGGTCAA TTATCAAAACG CGTTGCAACA ACGGTAACGA CGTCCGTAGC

4401 TGGTGTACAG CTCGTCTGTTT GGTATGGCTT CATTGAGCTC CGGTTCCCAA CGATCAAGGC GAGTTACATG ATCCCCCATG TTGTGCAAAA AAGCGGTTAG
ACCAACAGTGC GAGCAGCAAA CCATACCCGAA GTAAAGTCGAG GCCAAGGGTT GCTAGTTCCG CTCAATGTAC TAGGGGGTAC AACACGTTTT TTCGCCAATC

4501 CTCCTTCGGT CCTCCGATCG TTGTCAGAAAG TAAAGTTGGCC GCAGTGTAT CACTCATGGT TATGGCAGCA CTGCATAATT CTCTTACTGT CATGCCATCC
GAGGAAGCCA GGAGGCTAGC AACAGTCTTC ATTCAACCGG CGTCACAATA GTGAGTACCA ATACCGTCTGT GACGTATTAA GAGAATGACA GTACGGTAGG

4601 GTAAGATGCT TTTCTGTGAC TGGTGAGTAC TCAACCAAGT CATTCTGAGA ATAGTGTATG CCGCGACCGA GTTGTCTTTG CCCGGCGTCA ACACGGGATA
CATTCTACGA AAAGACACTG ACCACTCATG AGTTGGTTCA GTAAGACTCT TATCACATAC GCCGCTGGCT CAACGAGAAC GGGCCGCAGT TGTGCCCTAT

4701 ATACCGCGCC ACATAGCAGA ACTTTAAAAG TGCTCATCAT TGGAAAACGT TCCTCGGGGC GAAAACCTCTC AAGGATCTTA CCGCTGTTGA GATCCAGTTC
TATGGCGCGG TGTATCGTCT TGAAATTTTC ACCAGTAGTA ACCTTTTGCA AGAAGCCCCG CTTTTGAGAG TTCCCTAGAAAT GCGGACAACT CTAGGTCAAG

4801 GATGTAACCC ACTCGTGCAC CCAACTGATC TTCAGCATCT TTTACTTTCA CCAGCGTTTC TGGGTGAGCA AAAACAGGAA GGCAAAATGC CGCAAAAAAG
CTACATTGGG TGAGCACGTG GGTGACTAG AAGTCGTAGA AAATGAAAAG GGTCCGAAAAG ACCCACTCGT TTTTGTCTCTT CCGTTTTTACG GCGTTTTTTC

4901 GGAATAAGGG CGACACGGAA ATGTTGAATA CTCATACTCT TCCCTTTTCA ATATTATTGA AGCATTTATC AGGGTTATTG TCTCATGAGC GGATACATAT
CCTTATTCCC GCTGTGCCCT TACAACCTAT GAGTATGAGA AGGAAAAAGT TATAATAAAT TCGTAAATAG TCCCAATAAC AGAGTACTCG CCTATGTATA

5001 TTGAATGTAT TTAGAAAAAT AAACAATAG GGGTTCGGG CACATTTCCT CGAAAAAGTGC CACCTGACGT CTAAGAAAAC ATTATTATCA TGACATTAAC
AACTTACATA AATCTTTTTA TTTGTTTATC CCCAAGGCGC GTGTAAAGGG GCTTTTCACG GTGGACTGCA GATTCCTTTGG TAATAATAGT ACTGTAATTG

5101 CTATAAAAAAT AGGCGTATCA CGAGGCCCTT TCGTCTTCAA
GATATTTTTA TCCGCATAGT GCTCCGGGAA AGCAGAGTT

FIG. 24C

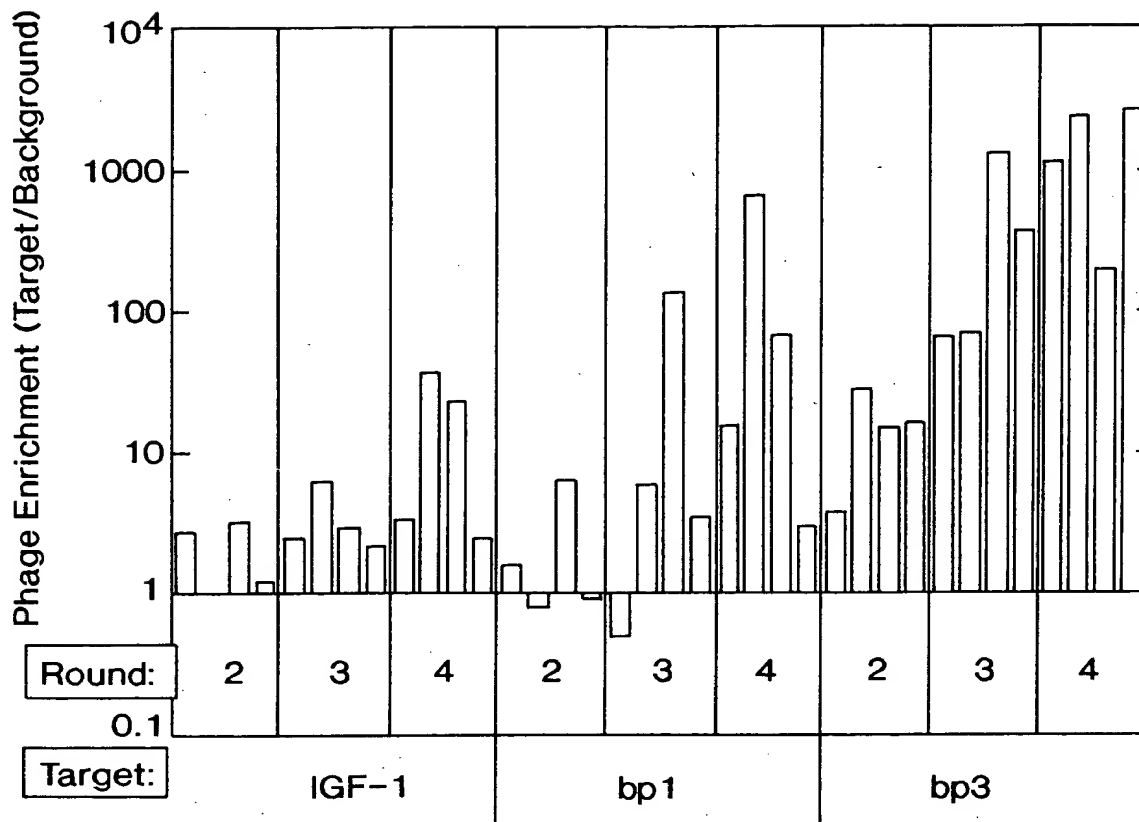


FIG. 25

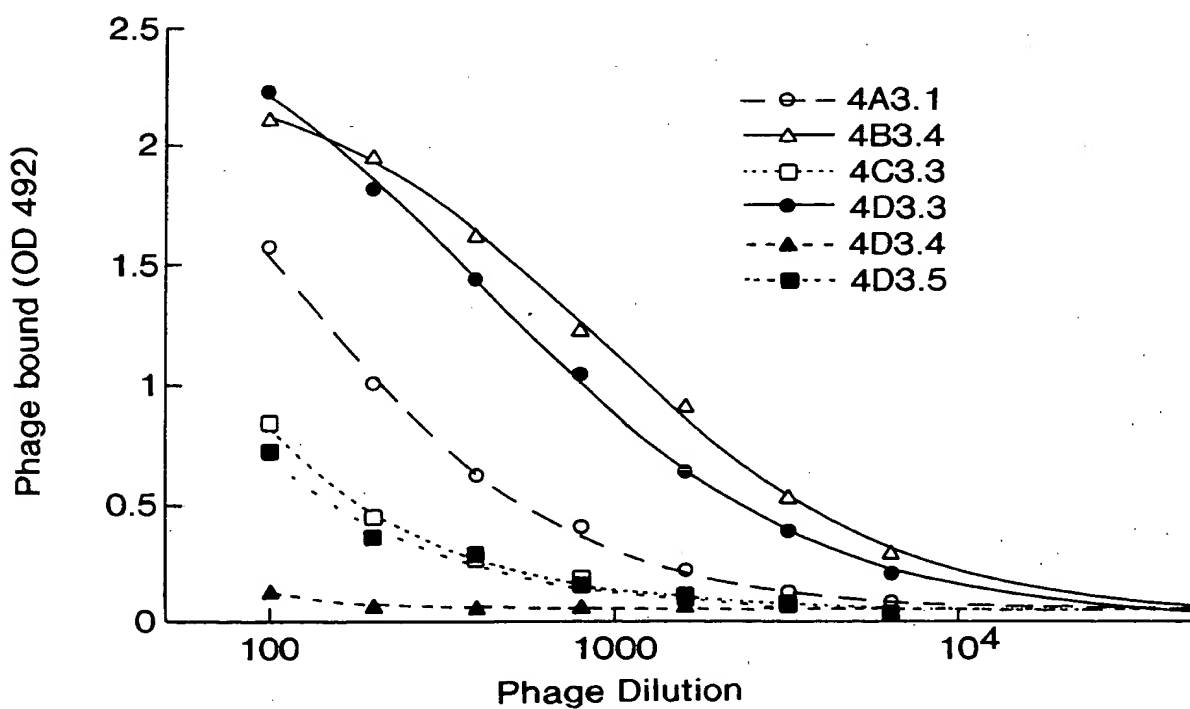


FIG. 26

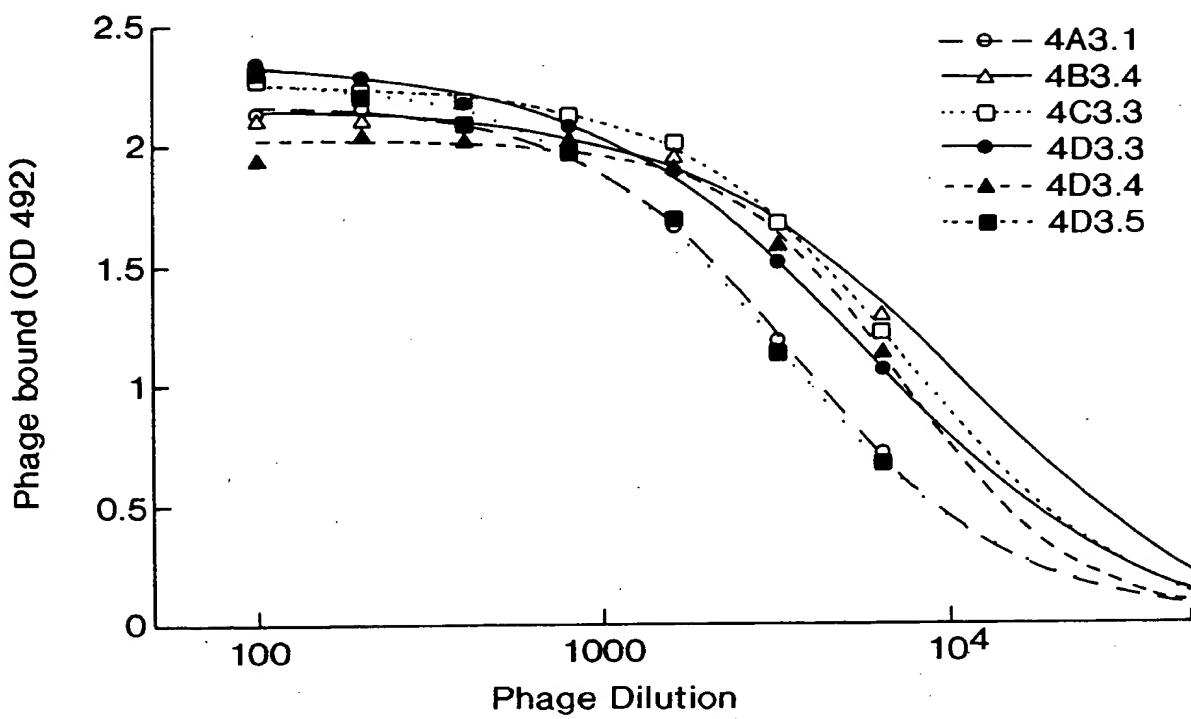


FIG. 27

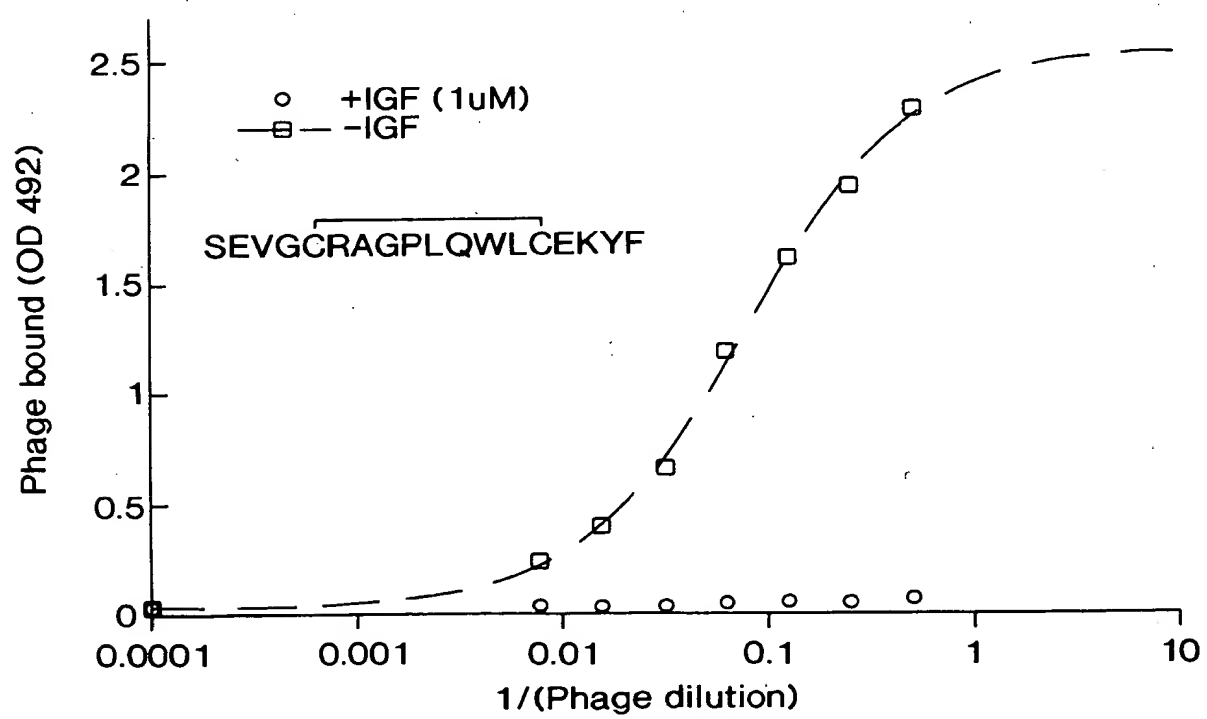


FIG. 28

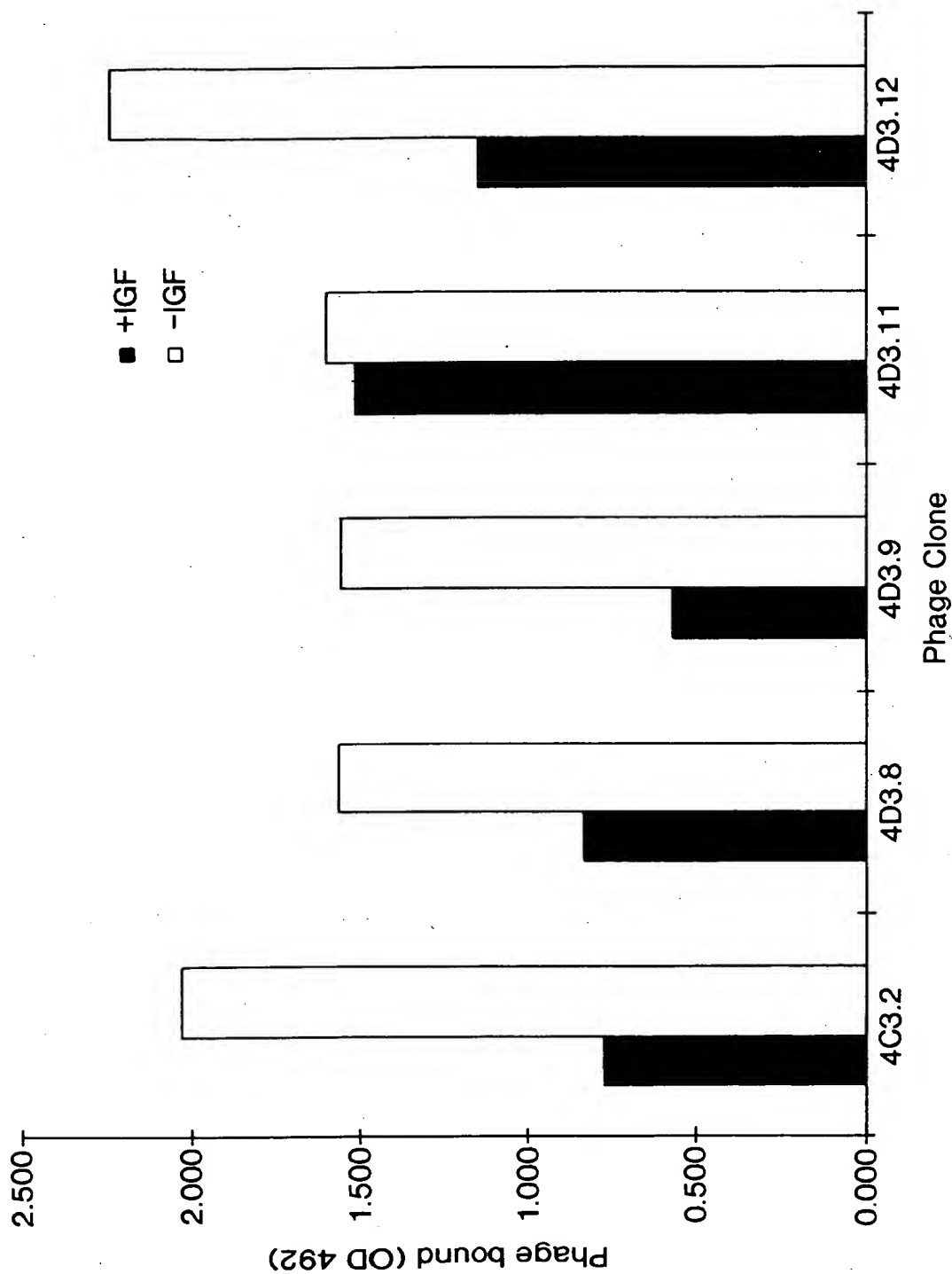


FIG. 29

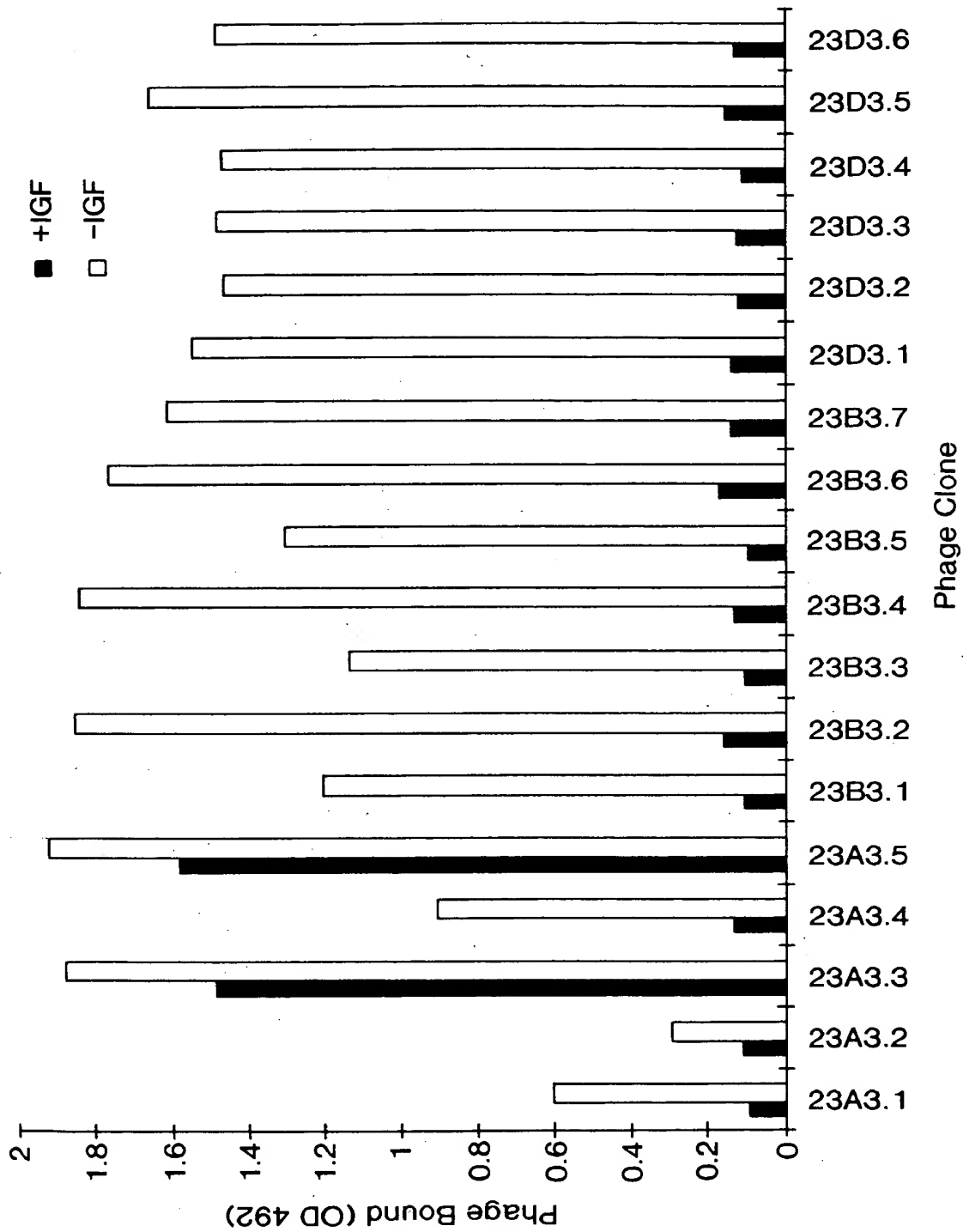


FIG. 30

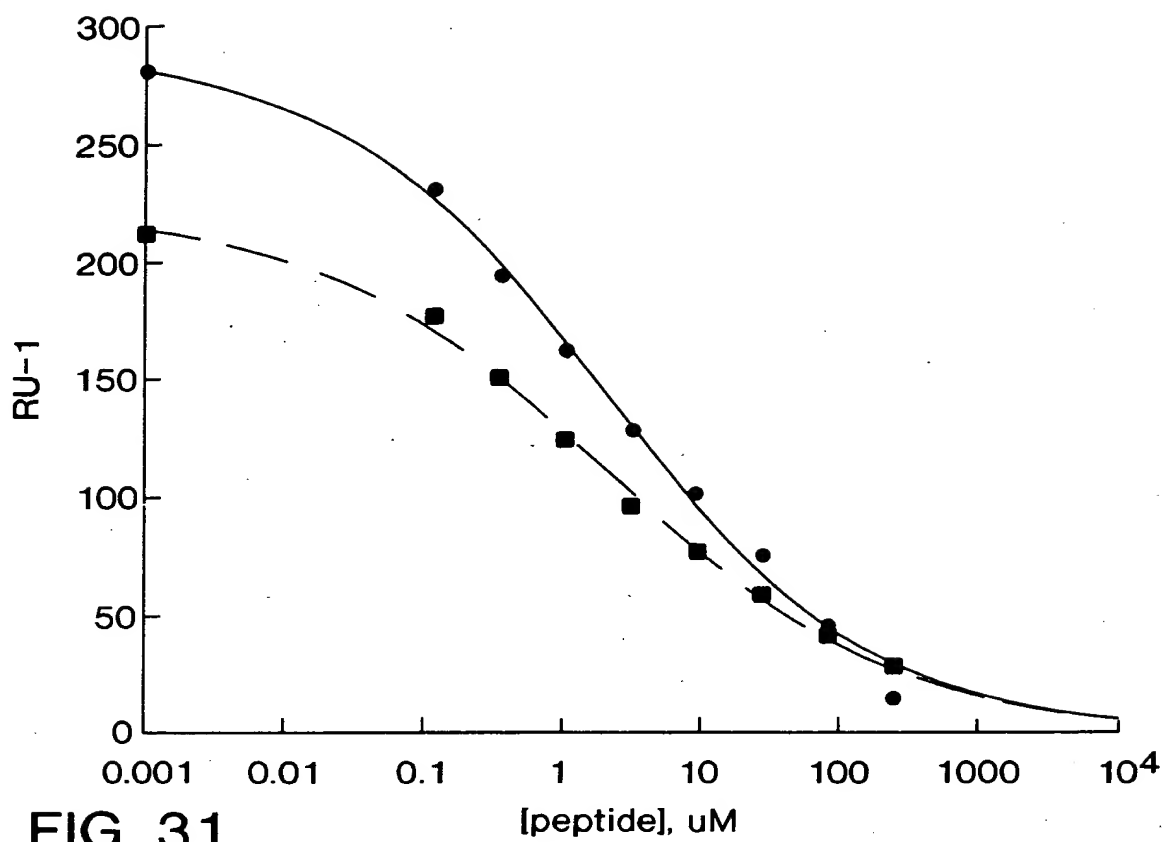


FIG. 31

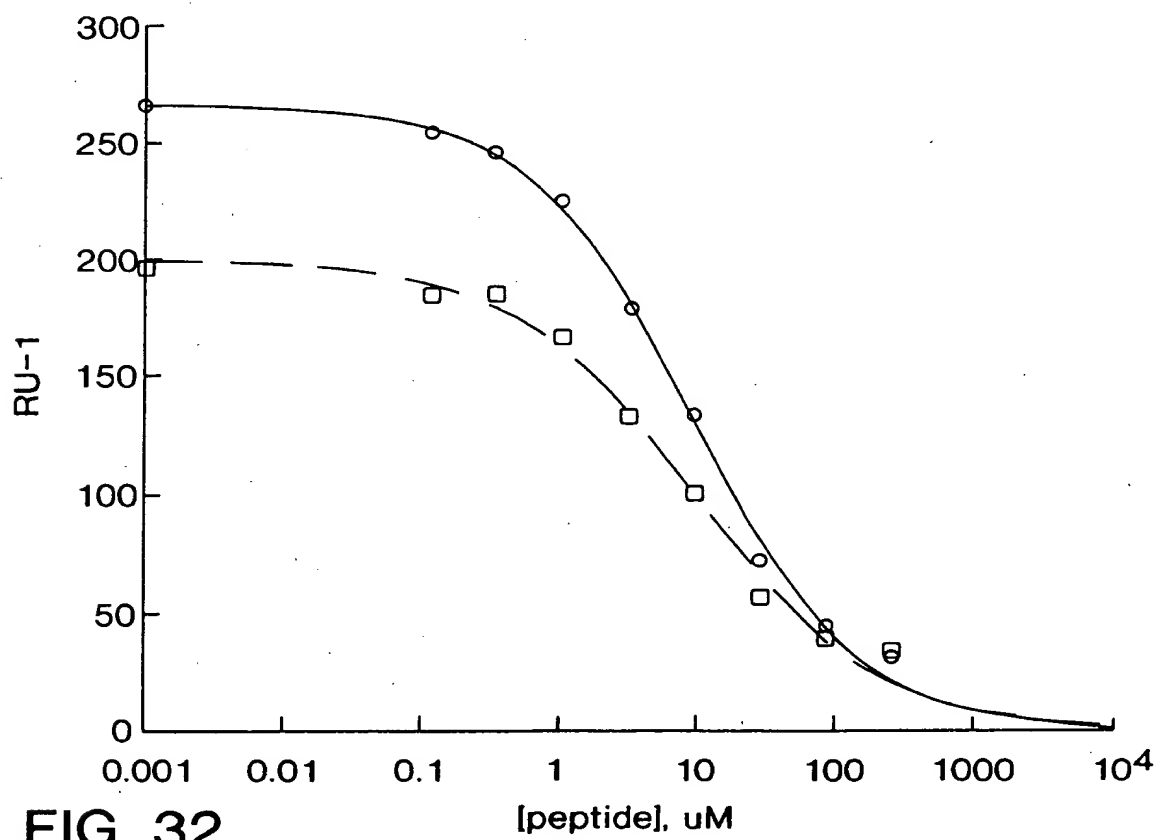


FIG. 32

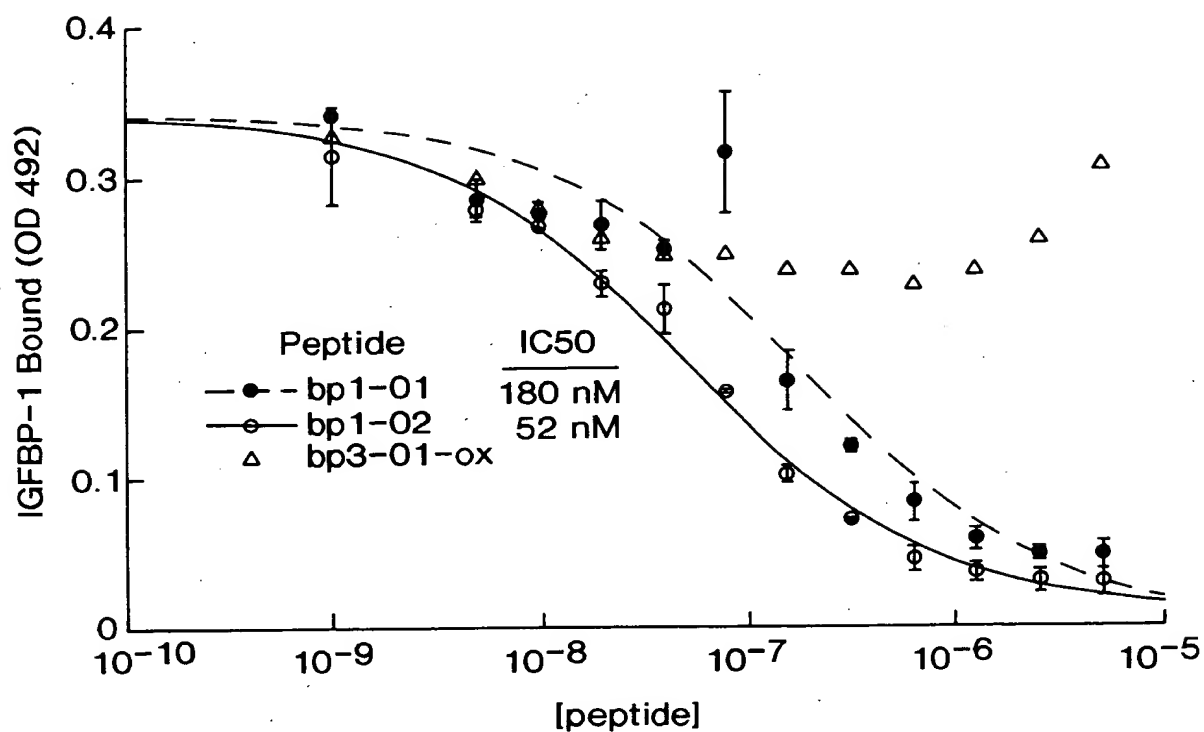


FIG. 33

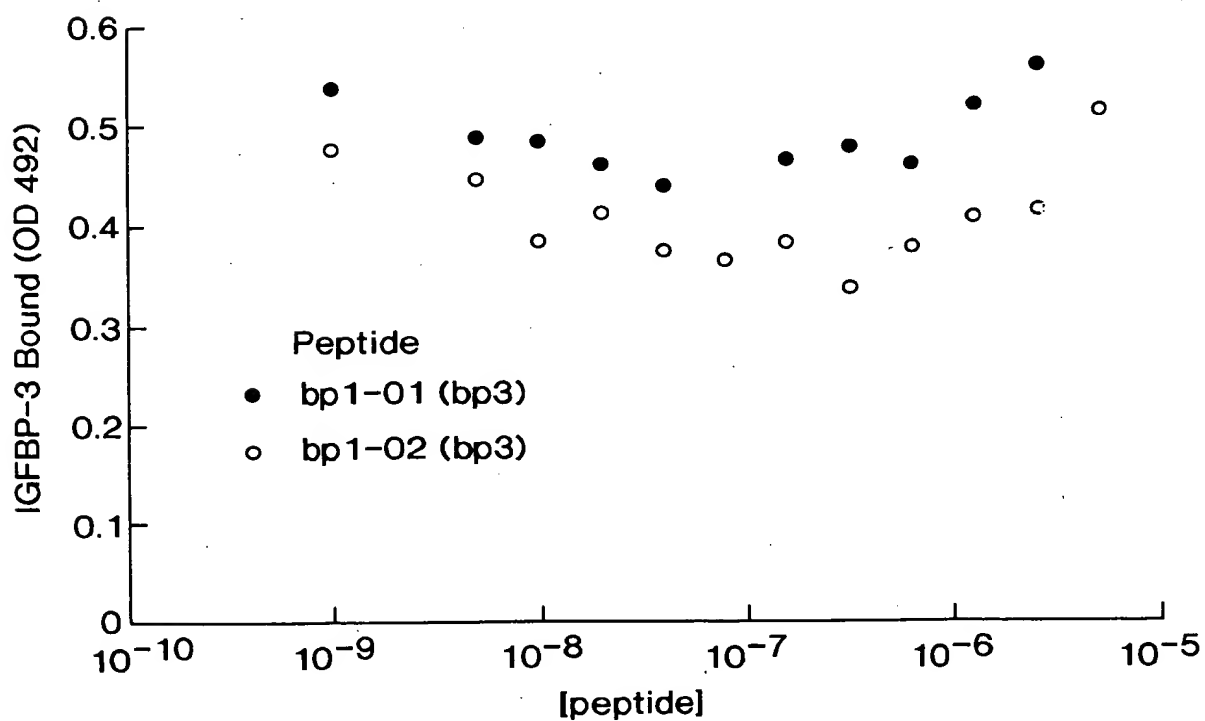


FIG. 34

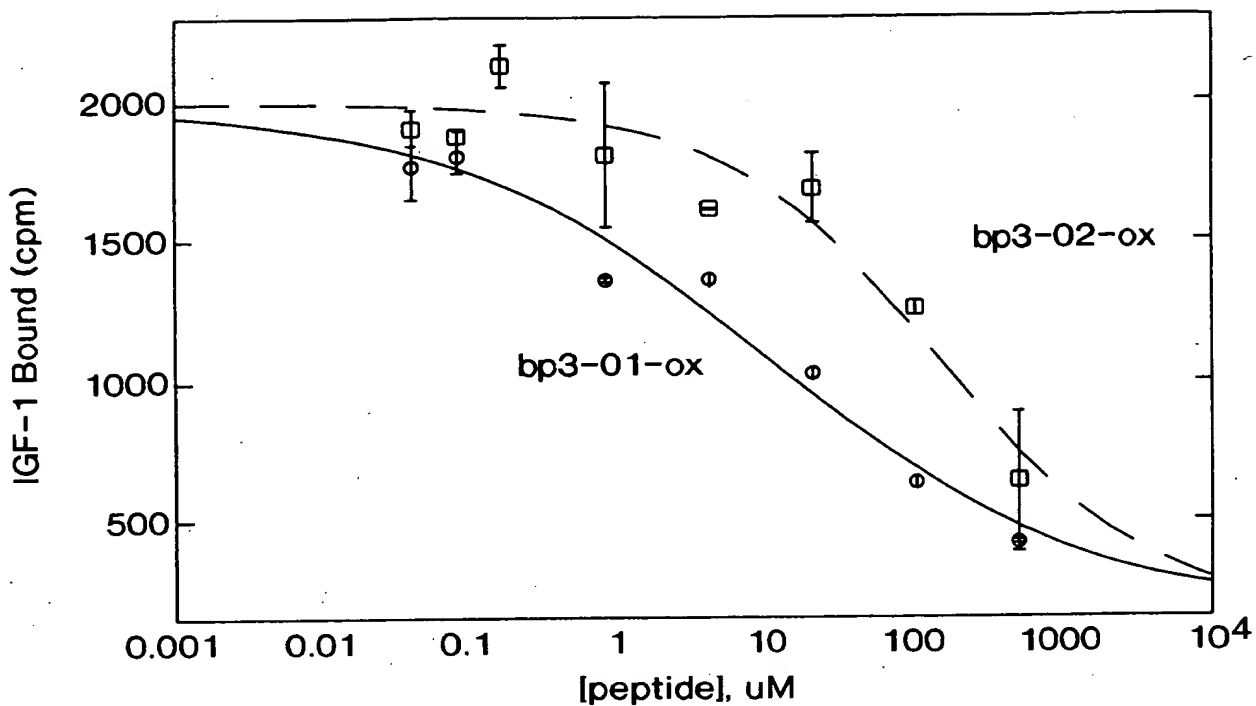


FIG. 35

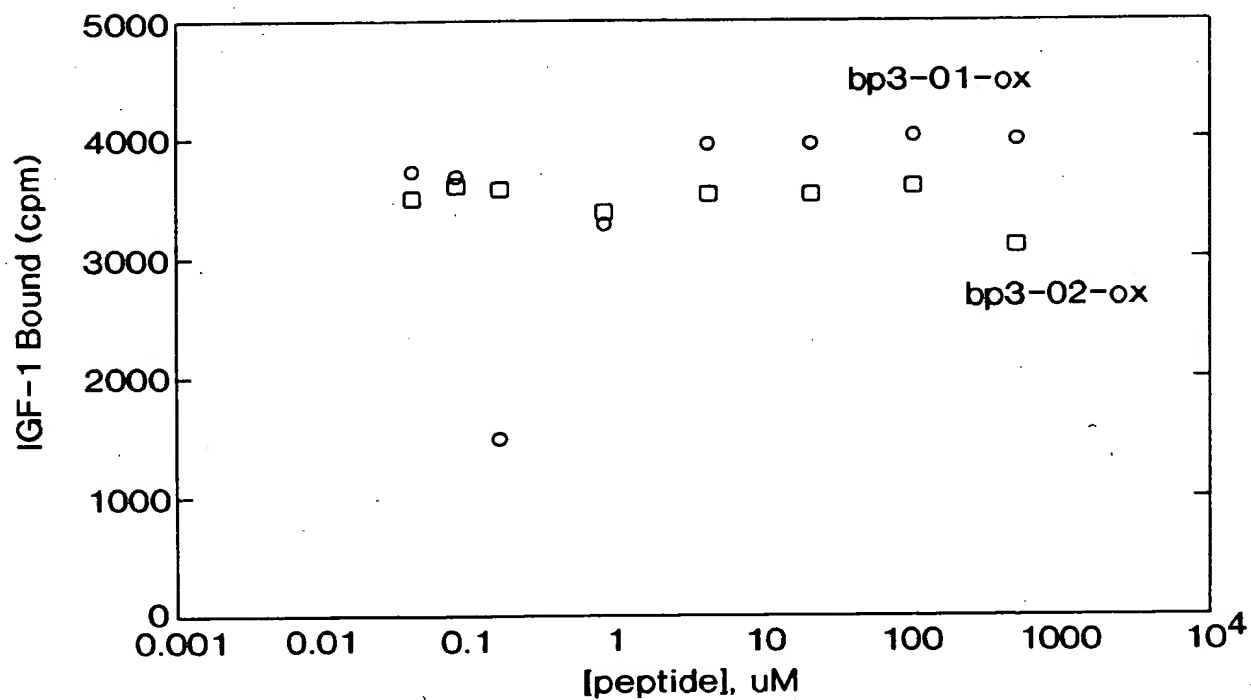


FIG. 36

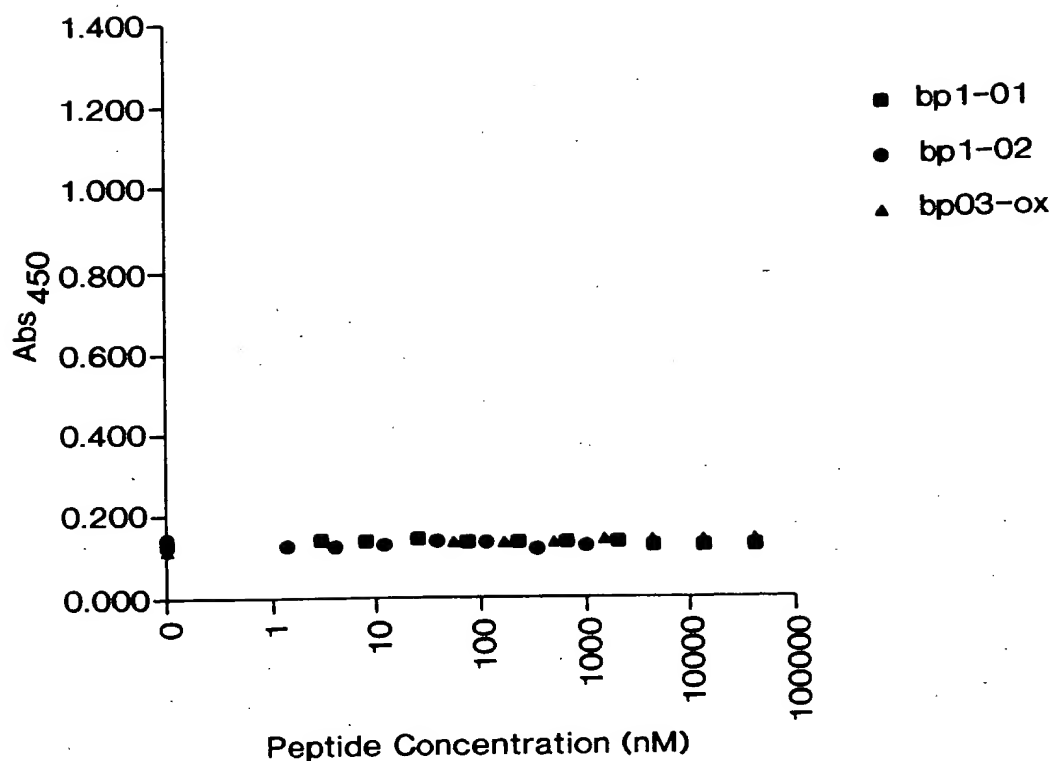


FIG. 37A

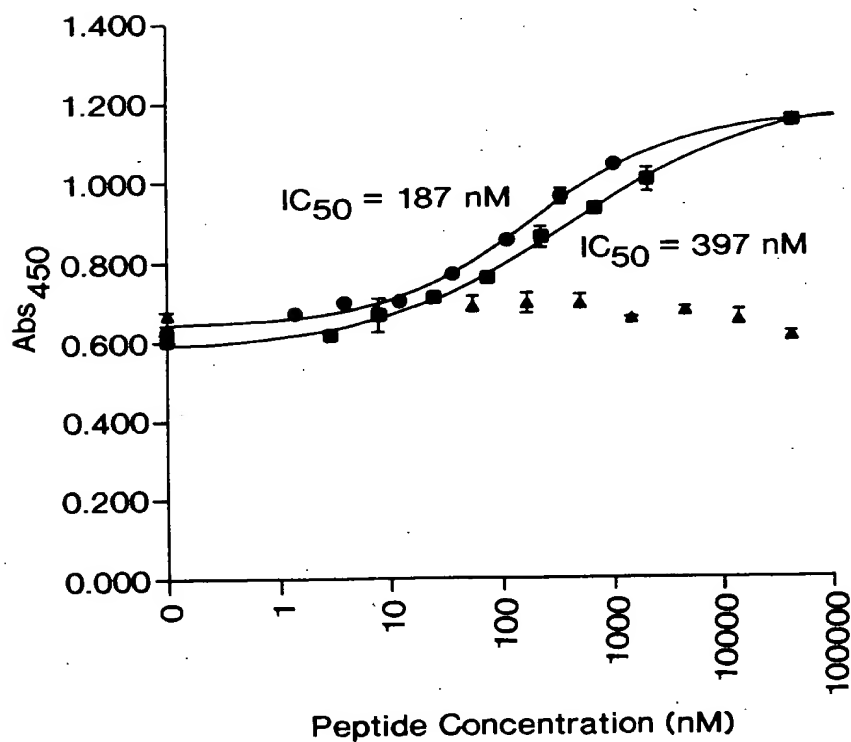


FIG. 37B

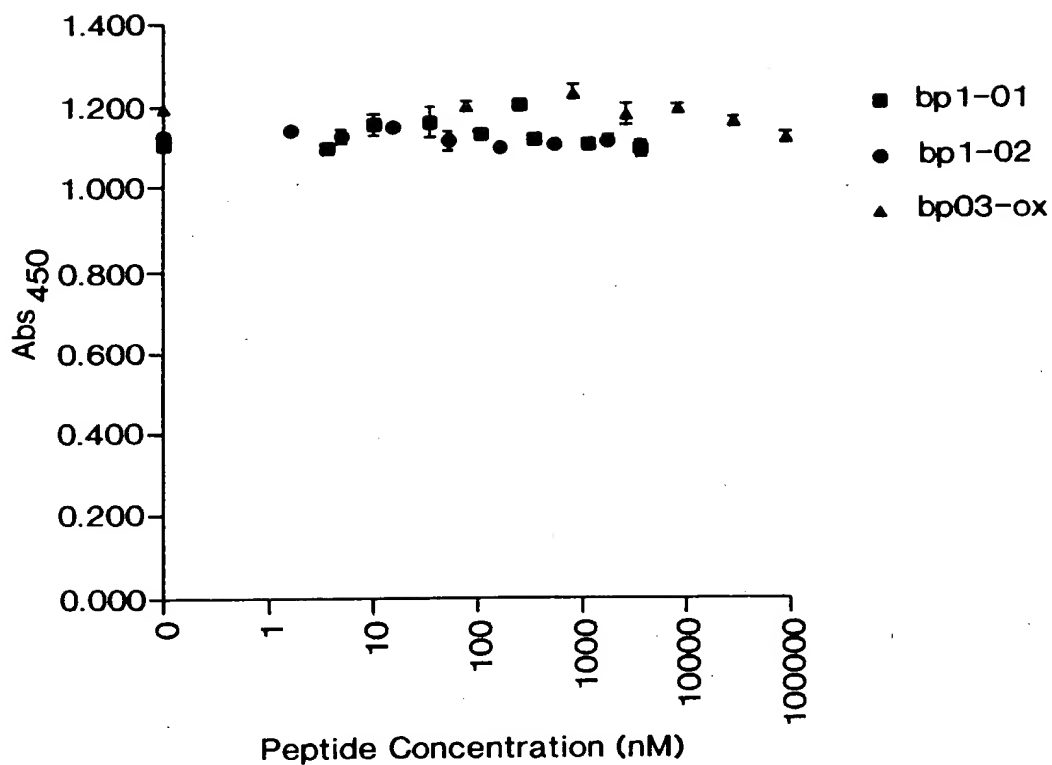


FIG. 37C

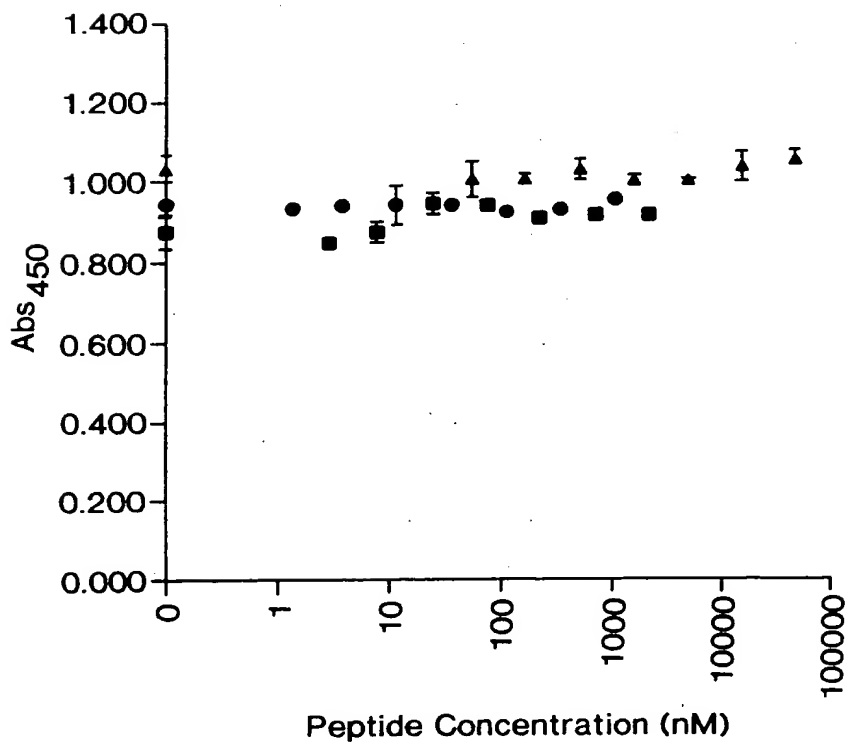


FIG. 37D

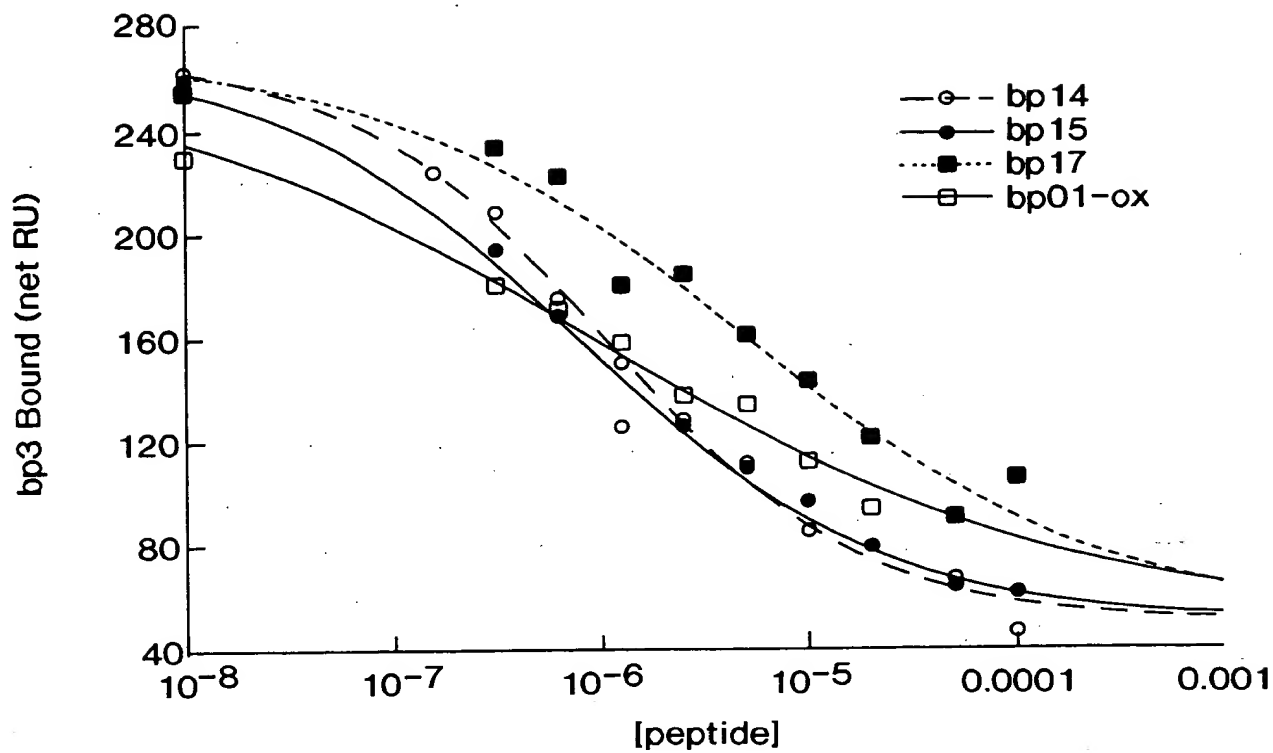


FIG. 38

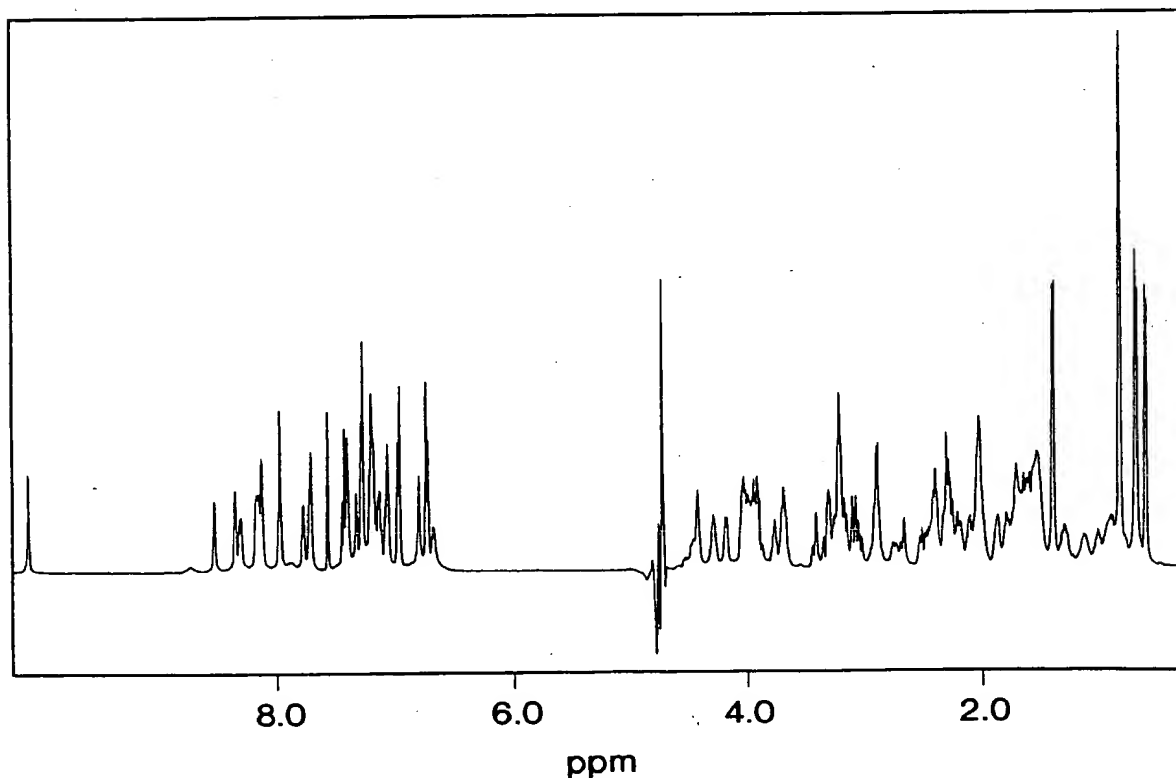


FIG. 39

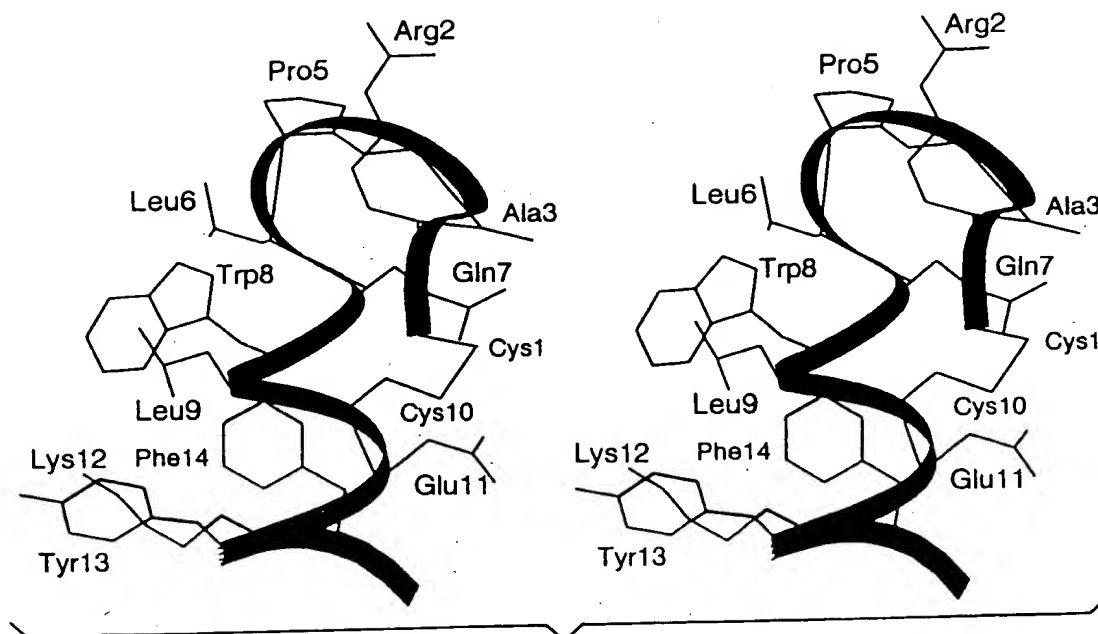


FIG. 40A

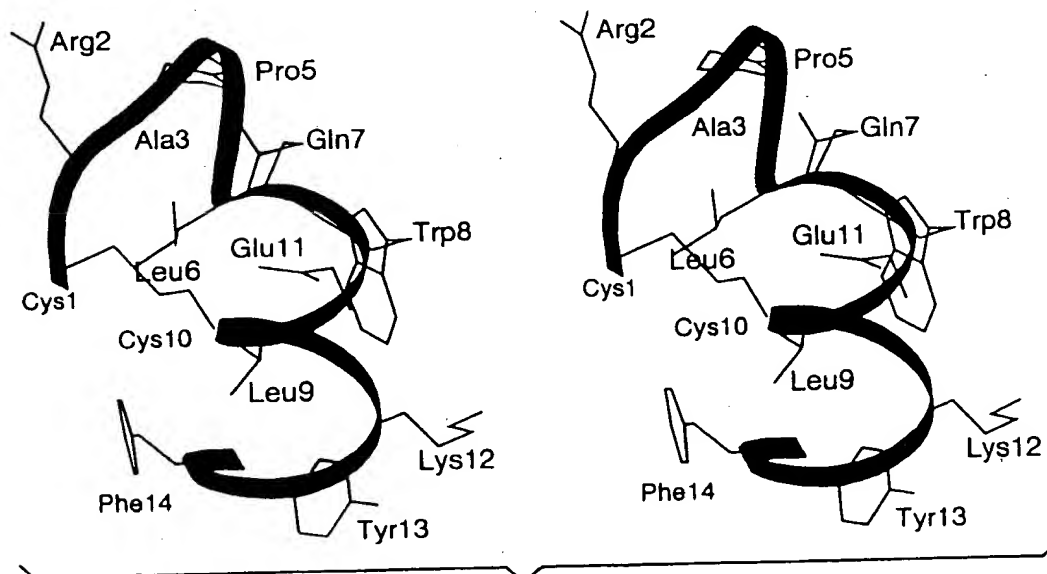


FIG. 40B

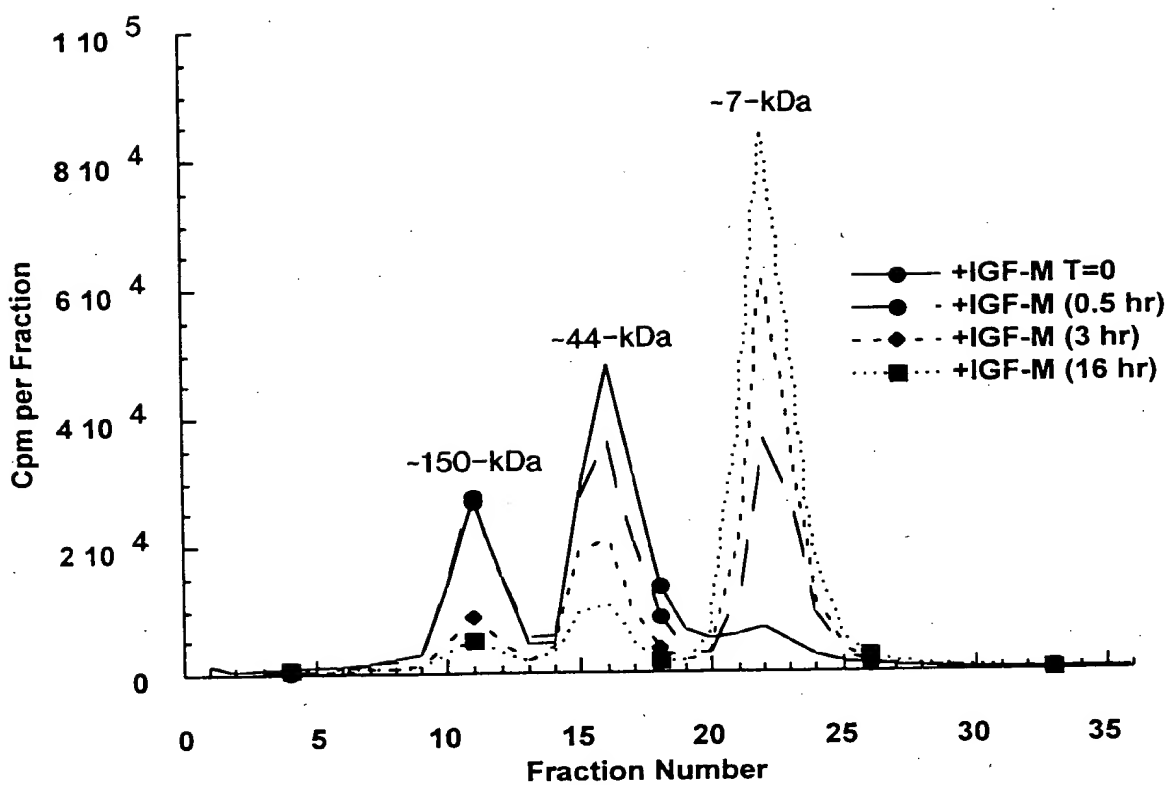


FIG. 41



Effect of IGF-I Treatment on Total IGF-I
(Mean \pm SE)

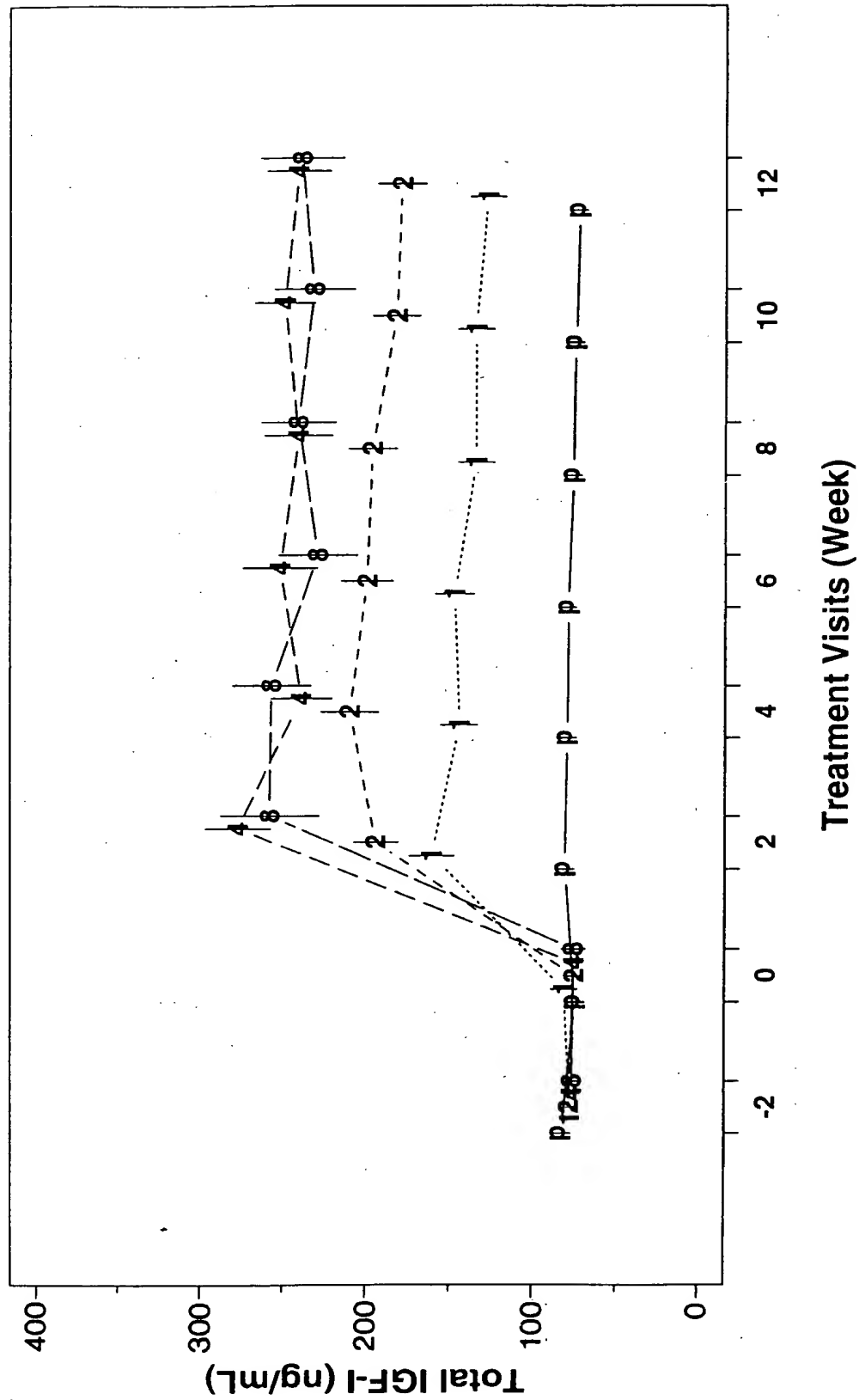
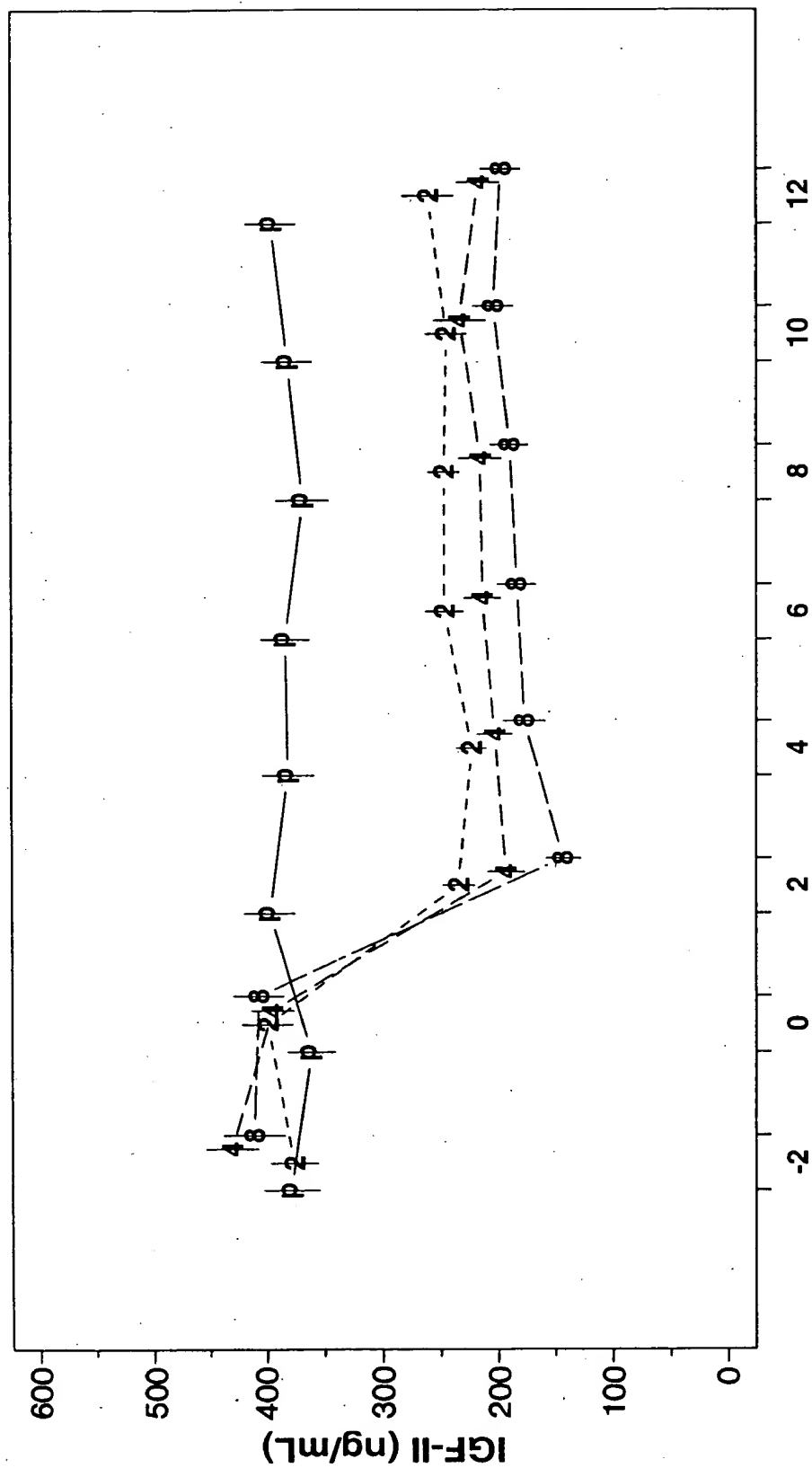


FIG. 42

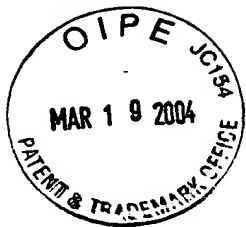
Effect of IGF-I Treatment on IGF-II

(Mean \pm SE)



Treatment Visits (Week)

FIG. 43



Effect of IGF-I Treatment on IGFBP-3

(Mean \pm SE)

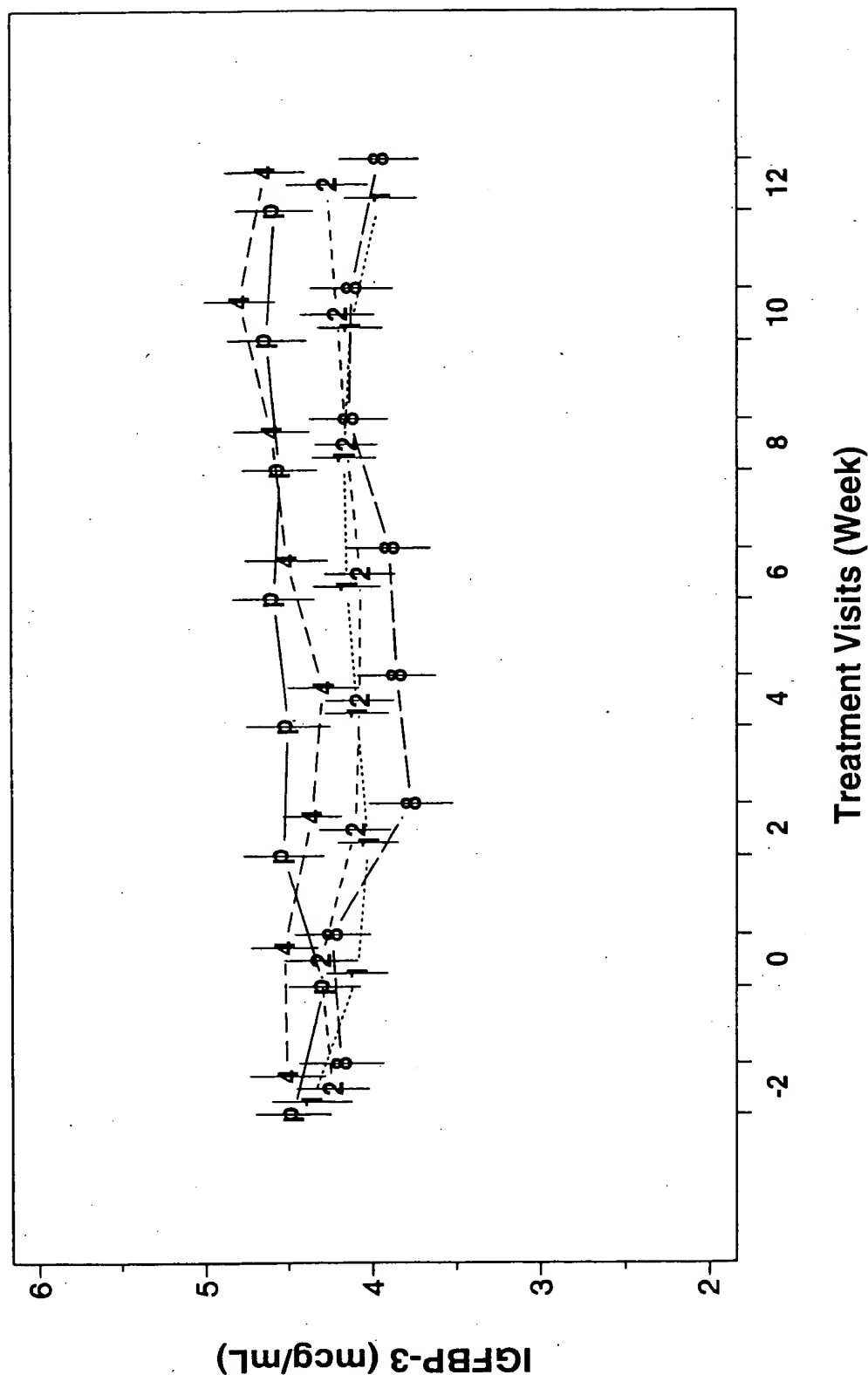


FIG. 44